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VOLUME 35 (old series Volume 92) APRIL 1946 NUMBER 4

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CORNEAL SECTION WITH LONG BEVEL AND CONJUNCTIVAL FLAP FOR CATARACT EXTRACTION

Preliminary Report

WALTER S. ATKINSON, M.D.
WATERTOWN, N. Y.

IN CATARACT extraction complications that formerly occurred at the time of operation have been reduced to a minimum by better anesthesia and improved operative technic. Attention is now directed more toward the prevention of postoperative complications.

The principal aims of the corneal section to be described are to prevent a leaky wound, with a shallow or empty anterior chamber, and to

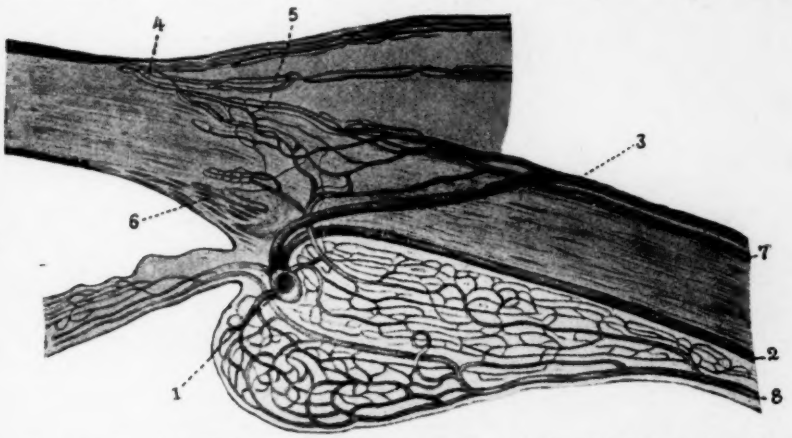

Fig. 1.—Blood vessels of the anterior segment (after Maggiore, L.: Ann. di ottol. e clin. ocul. **40**:317, 1917).

decrease the occurrence of postoperative hemorrhage into the anterior chamber.

Two features of the section designed to accomplish these aims are (1) a long bevel and (2) placement in avascular corneal tissue.

Firm suturing of the wound has practically eliminated prolapse of the iris, but the closure of the wound is often not sufficiently perfect to prevent a slow leak of aqueous or to prevent blood from entering the anterior chamber. It is generally conceded that to be effective sutures

Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., Nov. 12, 1945. At the time of presentation 50 cases comprised group 3.

must be placed in firm corneal or corneoscleral tissue and that such sutures can be more safely introduced before the section is made. The principle of introducing the suture before making the section was first advocated over fifty years ago by Suarez de Mendoza [1] and Kalt.[2] More recently, modifications by Liégard,[3] Stallard,[4] McLean [5] and others have emphasized this point.

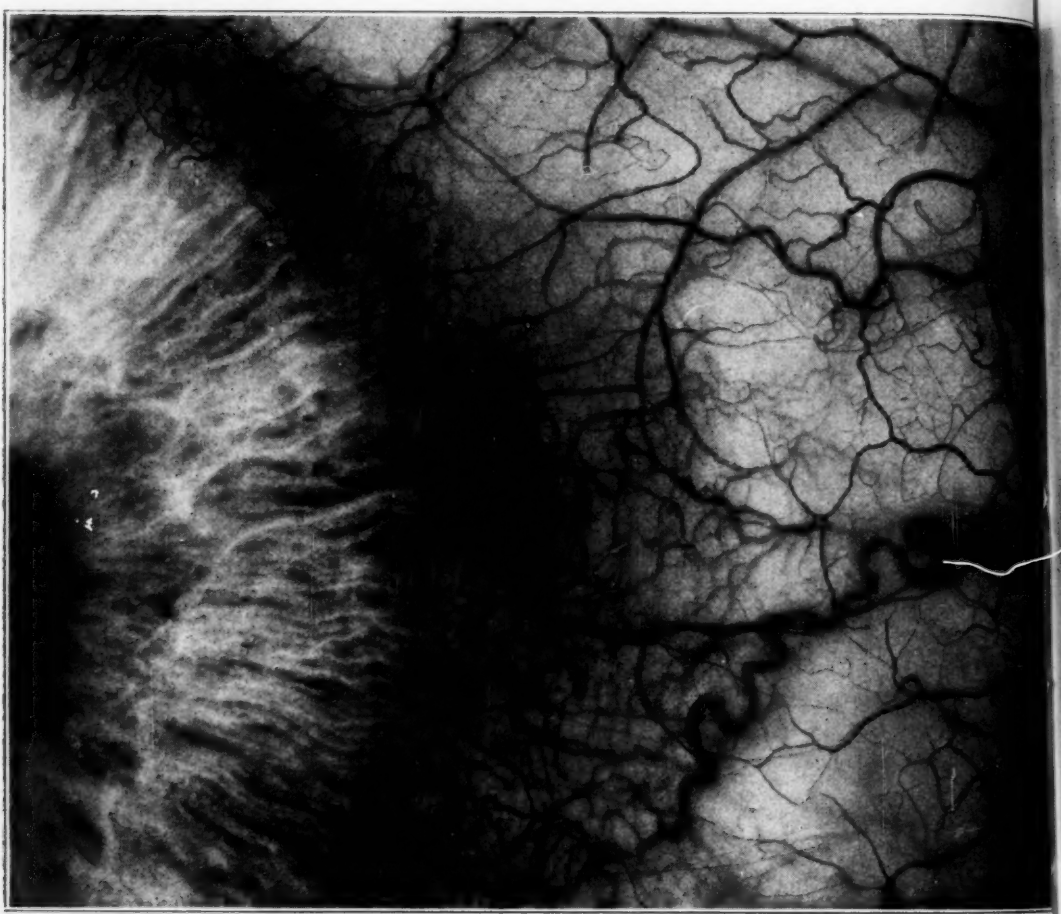

Fig. 2.—*A*, normal capillaries of the limbus. *B* (on facing page), engorgement of deeper set of arteries and the limbal capillaries such as might occur after cataract extraction (from Gartner, S.: Blood Vessels of the Conjunctiva, ARCH. OPHTH. **32**:464 [Dec.] 1944, figs. 2 and 5).

1. Suarez de Mendoza, F.: Nouveaux faits de suture de la cornée dans l'extraction de la cataracte, Bull. et mém. Soc. franç. d'opht. **10**:63, 1892.

2. Kalt, E.: On the Corneal Suture in Cataract Extraction, Arch. Ophth. **23**: 421, 1894.

The McLean suture satisfactorily fulfils the requirements, and it is easy to introduce. The chief advantage of the McLean suture over the Kalt, Liégard or Stallard type is that with it there is no overriding or lateral displacement.

The section is particularly important because it greatly influences and governs postoperative complications. Section with the Graefe knife when perfectly performed thrills even the seasoned surgeon. The most experienced operators, however, are not always able to obtain a perfect

Figure 2 *B*.

3. Liégard, H.: Une modification au procédé de suture de la cornée dans l'extraction de la cataracte, Ann. d'ocul. **149**:119, 1913.

4. Stallard, H. B.: A Corneo-Scleral Suture in Cataract Extraction: Its Technique and Advantages, Brit. J. Ophth. **22**:269, 1938.

5. McLean, J. M.: A New Corneoscleral Suture, Arch. Ophth. **23**:554 (March) 1940.

section with the Graefe knife. When the section is placed too far back, so that the vascular loops (fig. 1) are cut, bleeding complicates not only the operation but the convalescence. If the Graefe section is placed too far forward, a satisfactory conjunctival flap is not obtained. The importance of a conjunctival flap is so generally conceded that comment is unnecessary.

A large section is essential in order to allow easy extraction of the cataractous lens without rupture of the capsule or undue trauma. To obtain a well placed section, with a Graefe knife, of one-half the circumference of the cornea without injury to the iris is not always possible, particularly if the anterior chamber is shallow. Therefore, many surgeons now prefer to make a small initial incision with the Graefe knife or keratome and to enlarge it with scissors.

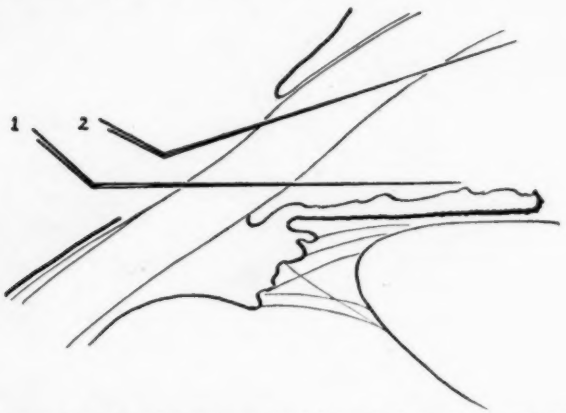

Fig. 3.—*1*, usual angle of keratome incision; *2*, long bevel obtained when the point of the keratome is directed away from the iris and toward the apex of the cornea.

Some of the advantages of the keratome for the initial incision have been pointed out by O'Brien.[6] An important point that O'Brien mentioned is that the section can be more easily and accurately placed.

Besides the advantages described by O'Brien, it is well known that the usual keratome incision is beveled, so that increased intraocular pressure tends to close the wound more tightly. If, therefore, the bevel is continued when enlarging the wound, a firmer closure is procured, so that the wound is less likely to leak. Although such a section with corneal ledge is contrary to orthodox teaching, it is the first point to be emphasized.

As shown diagrammatically in figure 3, if the point of the keratome is directed away from the iris and toward the apex of the cornea, the

6. O'Brien, C. S.: Comparison of the Keratome-Scissors and Graefe Knife Incisions for Cataract Extraction, Am. J. Ophth. **26**:508, 1943.

length of the bevel is increased. Such an incision tends to close more firmly and tightly when the normal intraocular pressure is restored or the intraocular pressure is increased. It should be noted, however, that with the long bevel placed well forward in the cornea it is essential to tumble the lens. Should the capsule rupture it is more difficult to express the lens matter; but since rupture of the capsule is not a frequent occurrence, it is not a serious consideration.

The hypermature cataract with a large, flat nucleus which does not tumble easily is more readily delivered head first, as suggested by Verhoeff.[7] In cases of this type an incision with a shorter bevel may be placed farther back. The possibility of hemorrhage is increased, and the closure may not be so firm; but to remove the lens in capsule seems more important than the increased risk of postoperative hemorrhage or a leaky wound.

Considerable investigation and discussion have failed to determine definitely the source and cause of all hemorrhages that occur after cataract extraction. There is, however, good evidence that the majority are from the newly formed vessels that cross the surface of the wound. It is generally agreed that most of the hemorrhages occur on the fourth to the sixth day. Henderson[8] and Collins[9] showed that it is on these days that new blood vessels grow across the wound, and Worth[10] pointed out that a slight rupture of the wound would tear the newly formed vessels. Vail[11] concurred in the opinion that the rupture of newly formed blood vessels at the section is the most frequent cause of hyphemia. A thorough review of the literature by DeVoe[12] and careful analysis of 95 cases of hemorrhage into the anterior chamber following cataract extraction in a series of 453 cases support the contention that the rupture of vessels which cross the surface of the wound is responsible for a large share of the hemorrhages.

It seems logical to expect less bleeding if the wound is located in tissue in which there are fewer and smaller vessels to rupture. Since the conjunctiva is not firmly attached to the cornea in the periphery (fig. 4), a flap can easily be made which exposes as much as 2 to 3 mm.

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7. Verhoeff, F. H.: A New Operation for Removing Cataracts with Their Capsules, Tr. Am. Ophth. Soc. **25**: 54, 1927.

8. Henderson, T.: A Histological Study of the Normal Healing of Wounds After Cataract Extraction, Ophth. Rev. **26**:127, 1907.

9. Collins, T.: Postoperative Complications of Cataract Extraction, Tr. Ophth. Soc. U. Kingdom **34**:41, 1914.

10. Worth, C., in discussion on Collins,[9] p. 67.

11. Vail, D.: On Hyphema After Cataract Extraction, Tr. Am. Ophth. Soc. **31**:496, 1933; Hyphema After Cataract Extraction, Am. J. Ophth. **24**:920, 1941.

12. DeVoe, G.: Hemorrhage After Cataract Extraction, Arch. Ophth. **28**:1069 (Dec.) 1942.

of cornea. This allows the section to be placed well forward in the cornea, so that the vascular loops are avoided. Placing the section in avascular corneal tissue is the second point to be emphasized.

TECHNIC OF OPERATION

The technic of the corneal section with long bevel and conjunctival flap is as follows:

To dilate the pupil, 4 per cent homatropine hydrobromide is instilled in the eye one hour before operation. Anesthesia, as previously described,[13] is produced by the instillation of 0.5 per cent tetracaine hydrochloride and several drops of epinephrine hydrochloride 1:1,000. Procaine hydrochloride, 2 per cent, with

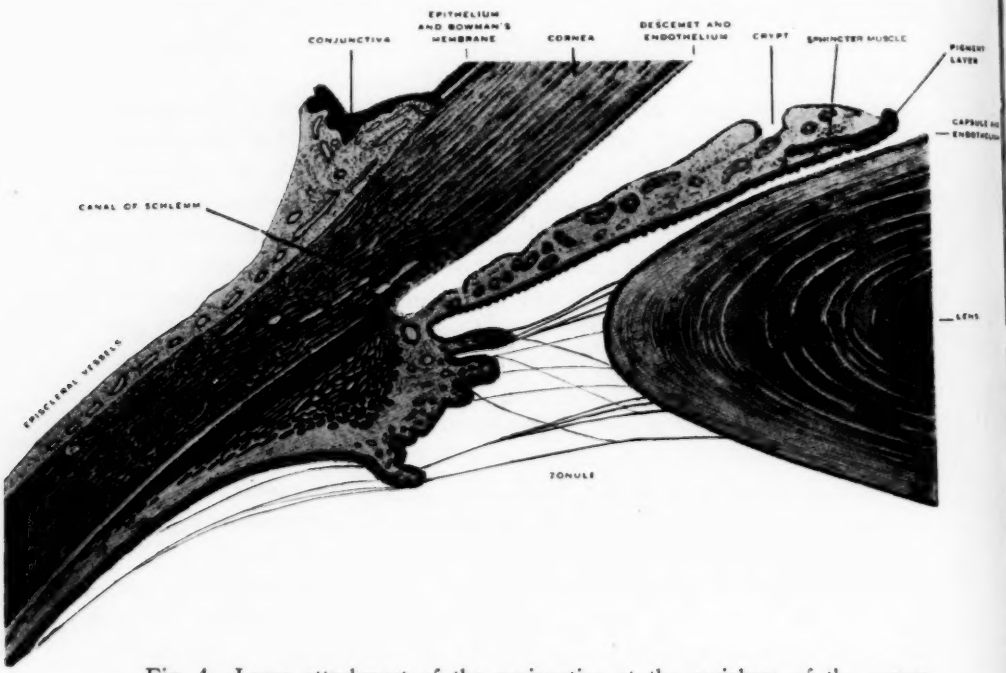

Fig. 4.—Loose attachment of the conjunctiva at the periphery of the cornea (from Wolff, E.: The Anatomy of the Eye and Orbit, Philadelphia, The Blakiston Company, 1940).

epinephrine hydrochloride is used to produce akinesia and for the cone injection. An injection of procaine is also made along the superior rectus muscle to avoid pain caused by the introduction of the suture in the superior rectus.

To make the conjunctival flap, a snip is made in the conjunctiva with blunt-pointed scissors about 4 mm. above the corneal margin. The cut edge of the conjunctiva is picked up, care being taken to avoid the subconjunctival tissue. The blade of the scissors is then slid under the conjunctiva, and a flap sufficiently

13. Atkinson, W. S.: Local Anesthesia in Ophthalmology, Arch. Ophth. **30**: 777 (Dec.) 1943.

large to cover the wound is made. Little bleeding occurs if the subconjunctival tissue and the vessels are avoided. The thin conjunctival flap may be turned down over the cornea with practically no dissection. The conjunctiva is more firmly adherent temporally as the 180 degree meridian is approached, and not so much cornea is exposed, either temporally or nasally, as there is above. The amount of cornea exposed can be increased by a little dissection with scissors, knife or Green corneal splitter.

A McLean [5] type of suture is introduced above at 12 o'clock. One suture is usually sufficient, but if more are indicated they may be introduced after the central one is tied. For the initial incision a straight-sided keratome, 4 to 5 mm. wide (fig. 5) is used. It is introduced at the site of the suture, and at an angle to produce a long bevel. The wound is enlarged with keratome as it enters the anterior chamber and as it is partially withdrawn and reintroduced with a sawing motion. No aqueous escapes as the keratome is introduced, so that several strokes can usually be made and the wound enlarged halfway to the 180 degree meridian

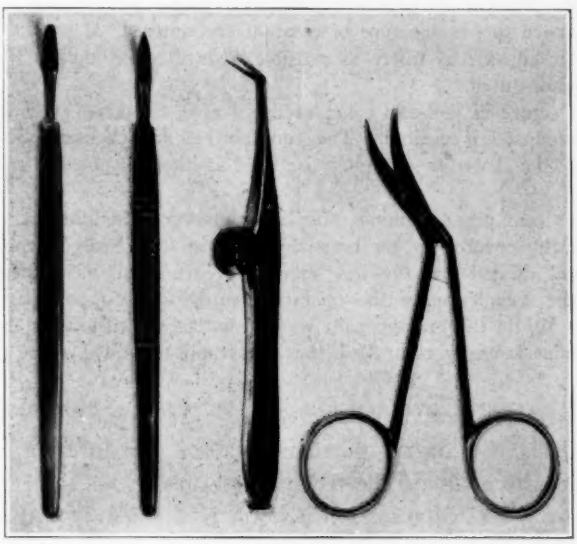

Fig. 5.—Left to right: Blunt-pointed keratome; straight-sided keratome; de Wecker scissors, both blades pointed; modified Walker scissors.

before the aqueous escapes. If the aqueous is lost, a blunt-pointed, straight-sided keratome (fig. 5) is used to complete the enlargement of the wound because it can be introduced more easily and safely into a shallow or empty chamber. A straight-sided keratome is preferred because so little counterpressure is required to introduce it, aqueous is rarely lost and it makes a straight, linear cut. The longest bevel is made in the middle third of the section and extends from 10.30 to 1:30 o'clock, where prolapse of the iris and leaks most frequently occur. The wound is further enlarged with scissors to one-half the circumference of the cornea. The amount of bevel is decreased as the 180 degree meridian is approached because if the long bevel were continued to the 180 degree meridian the wound would not open widely enough to allow easy extraction of the lens. The bevel may be increased or decreased with scissors by tipping the inside blade toward or away from the cornea.

It should be noted that it is more difficult to begin the enlargement of the wound with scissors when there is a long bevel. If, however, the scissors are well opened, so that the blade that enters the anterior chamber clears the broad edge of the wound produced by the long bevel, little difficulty will be experienced. Short snips should be made with the scissors to avoid buckling the cornea. A modified Walker scissors (fig. 5) has been found to be the most satisfactory in enlarging the wound.

In many instances, with the pupil dilated, the iris is practically covered above by the corneal ledge. If not, one to three iridotomies are made at 12:00, 10:30 and 1:30 o'clock, respectively, using de Wecker scissors which have the two blades pointed and of the same length (fig. 5). The corneal flap is raised, the iris drawn down a little with the points of the scissors and a small hole snipped in the iris close to the upper corneal lip. No forceps are used to grasp the iris.

For immature or mature cataracts the anterior capsule is grasped well below with the Elschnig modification of the Kalt forceps, and the lens is tumbled and extracted with pressure and traction. The technic and method of extraction, however, are changed to suit the type of cataract encountered. The aim is to remove the cataract in capsule as safely as possible, regardless of the method or combination of methods used.

After the suture is tied and toilet of the wound completed, other sutures may be safely introduced if desired. The conjunctival flap is smoothed out but not sutured, and the anterior chamber is filled with half-normal saline solution or air.

A 0.25 per cent physostigmine salicylate ointment is instilled except when the iris is practically covered by the corneal shelf. In such cases atropine is used to keep the pupil dilated and the iris under the corneal shelf. When atropine is instilled at the completion of the operation, practically no postoperative pain is experienced. While the crampy pain which regularly occurs after the instillation of physostigmine is easily controlled, it is preferable not to have the pain.

EVALUATION OF TECHNIC

An analysis of cataract extractions done by different methods is given in order to evaluate the technic described.

A series of 300 cataract extractions is divided into three groups. In group 1 are 100 consecutive extractions in which a corneoscleral section with conjunctival flap was made with a Graefe knife. Corneoscleral sutures were introduced after the section. In group 2 are 100 consecutive extractions in which a conjunctival flap was first made. A Stallard type of suture was introduced before the section, which was made with a keratome and enlarged with scissors.

In group 3 are 100 consecutive extractions in which a conjunctival flap was first made. A McLean type of suture was introduced, and a long-beveled section was made with keratome and enlarged with keratome and scissors.

As the series progressed, more careful notes were made with regard to leaky wounds and blood in the anterior chamber. If the chamber was observed to be just a little shallow at one dressing, the case was recorded as one of a leaky wound. Any blood in the anterior chamber,

such as a small blood stain of the iris, was listed as hemorrhage in the anterior chamber. This may in a measure account for the comparatively small decrease in the number of leaky wounds and hemorrhages recorded in groups 2 and 3 as compared with the number in group 1, for in the first group such minor leaks and hemorrhages were not all recorded. Therefore the tables give an erroneous impression in regard to the leaks and hemorrhages, particularly in group 3. Actually, in group 3 there was only 1 empty chamber and 1 hemorrhage large enough to prolong the patient's stay in the hospital.

COMMENT

As shown in table 1, there were no serious complications due to leaky wounds in groups 2 and 3. In group 1 a leaky wound was a

TABLE 1.—*Visual Results in 33 Cases With Leaky Wounds in a Series of 300 Cataract Extractions*

Visual Acuity	Group 1 (100 Cases)		Group 2 (100 Cases)	Group 3 (100 Cases)
20/15	5		8	2
20/20	5		2	3
20/25	5		1	4
20/200*	1	Detachment of retina		
10/200	1	Secondary glaucoma and diabetic retinopathy		
Total.....	17	17%	11 11%	9 9%

* Vision was 20/30 until detachment occurred, eleven months after operation.

serious complication in 2 cases. In 1 case vision was 20/30 until detachment of the retina occurred, eleven months later, after which it was reduced to 20/200. The leak was considered responsible for the

TABLE 2.—*Visual Results in Cases of Hemorrhage in Anterior Chamber Which Occurred in a Series of 300 Consecutive Cataract Extractions*

Visual Acuity	Group 1 (100 Cases)	Group 2 (100 Cases)	Group 3 (100 Cases)
20/15	7	6	2
20/20	3	2	2
20/25	5	2	4
Died in hospital	0	1	0
Total number of cases with hyphemia.....	15 15%	11 11%	8 8%

detachment, because vitreous was pinched in the wound at the site where it opened. In the second case secondary glaucoma developed. A cyclodialysis controlled the intraocular pressure; but diabetic retinopathy was also present and accounted for some loss of vision, so that final vision was 10/200.

The visual results shown in table 2 indicate that hyphemia is not a serious complication. Vision was affected little, but convalescence in some instances was prolonged, so that several days were added to the stay in the hospital. In groups 2 and 3 all but 2 of the hemorrhages

TABLE 3.—*Data on Three Groups of Cataract Extraction*

	Group 1 *	Group 2 †	Group 3 ‡
Leaky wounds	17%	11%	9%
Hemorrhage in anterior chamber	15%	11%	8%
Intracapsular extractions	75%	81%	85%
Unintentional rupture of capsule	20%	10%	8%
Round pupil	64%	80%	95%
Vitreous presented	2%	1%	1%
Prolapse of iris	2%	1%	1%
Secondary glaucoma	2%	2%	1%
Detached retina	1%	0%	0%

* Group 1 (100 consecutive cataract extractions): A corneoscleral section with conjunctival flap was made with a Graefe knife. Corneoscleral sutures were introduced after the section.

† Group 2 (100 consecutive cataract extractions): A conjunctival flap was first raised. A Stallard type of suture was introduced before the section, which was made with a keratome and enlarged with scissors.

‡ Group 3 (100 consecutive cataract extractions): A conjunctival flap was first raised. A McLean type of suture was introduced and a long-beveled section made with the keratome and enlarged with keratome and scissors.

TABLE 4.—*Visual Results with Three Methods of Cataract Extraction*

Visual Acuity	Group 1 (100 Cases)	Group 2 (100 Cases)	Group 3 (100 Cases)
20/15	43	43	49
20/20	17	35	21
20/25	26	19	13
20/30	2	5	3 (1 High myopia with chorioretinal changes; 1 Corneal opacity (old); 1 Acute glaucoma; iridectomy 6 yr. before cataract)
20/40	3	2	6 (3 Central chorioretinitis (old); 2 High myopia with changes of chorioretinitis; 1 Vitreous opacities)
20/50	4 (1 High myopia, chorioretinitis; 2 Chorioretinitis (old); 1 Iridocyclitis)		
20/70	.....	1 Old corneal opacity	
20/100	1 Chorioretinitis (old)	2 Chorioretinitis (old)	3 (1 Central chorioretinitis (old); 1 Corneal opacities (old); trachoma; 1 Corneal dystrophy (old))
20/200 or less	4 (1 Retinal detachment; 1 Diabetic retinopathy; 1 Diabetic retinopathy and secondary glaucoma; 1 Chorioretinitis (old))	1 Cosmetic ext. (blind eye) iridocyclitis and secondary glaucoma	4 (1 Albino with nystagmus; 1 Central retinitis; 1 Macular degeneration (both eyes); 1 Iridocyclitis)
		1 Died in hospital	1 Patient died before vision determined
	100	100	100

were small, in some cases being only a slight blood stain of the iris; this is a great improvement over the results of the 100 extractions in group 1.

Table 3 summarizes the data for the three groups and shows a definite improvement as the series progressed. In groups 2 and 3 more freedom was allowed the patients during convalescence; this added greatly to their comfort and caused no apparent harm to their eyes.

In table 4 are given the visual results. In each group is included the usual number of complicated cataracts in which there was some preexisting condition that affected the sight. To evaluate properly the three methods of cataract extraction, such complicated cases probably should be omitted.

In the three groups, there was a progressive increase in the percentage of cases in which more acute vision was obtained. In group 1 there were 60 per cent in which vision was 20/20 or better; in group 2, 68 per cent, and in group 3, 70 per cent.

Although 7 cases with high myopia and fluid vitreous are included in groups 2 and 3, there was no case in which vitreous presented during or directly after the section, as is occasionally seen with the Graefe section. Possibly the reason is that the globe is distorted so little with the section made with the keratome and scissors as compared with the section made with the Graefe knife.

It is appreciated that with such a small series definite conclusions cannot be drawn; however, a careful analysis of even a few cases is of value.

CONCLUSION

The long-beveled corneal section with conjunctival flap made with keratome and scissors is safe.

With it the number of postoperative leaky wounds was reduced in the series reported here.

Hyphemia still occurred, but the hemorrhages were smaller and less frequent.

129 Clinton Street.

REFRACTION BY THE ASTIGMATIC EYE

HARRY EGGERS, M.D.
NEW YORK

REGULAR ASTIGMATISM

WHEN the refracting power of the eye as a whole, instead of being identical in all meridians, changes gradually from one meridian to the next by uniform increments, and when each meridian has a uniform type of curve throughout the refracting zone, the condition is known as regular astigmatism. This is the condition that ordinarily is corrected by a cylindric or spherocylindric spectacle lens.

Regular astigmatism usually is caused by a toroidal, instead of a spherical, curvature of one or more refracting surfaces of the eye. Occasionally it results from an oblique or tilted position of the lens with respect to the optic axis. Other causes are rare.

When two or any larger number of cylindric or spherocylindric refracting surfaces are combined with their axes in varying positions with respect to each other, the result always will be a spherocylindric equivalent, in which the meridian of greatest curvature is at right angles to the meridian of least curvature. Consequently, it does not matter if, in one or more of the refracting surfaces of the eye, the meridian of greatest curvature actually is crossed obliquely by the meridian of least curvature, instead of at a right angle. The resultant effect always is that of a spherocylindric combination in which the meridians of greatest and least curvature are arcs of circles at right angles to each other. The intervening meridians will have a correspondingly greater or lesser curvature, but they will be the arcs of ellipses and not the arcs of circles.

PATH OF LIGHT THROUGH AN ASTIGMATIC EYE

A beam of light that enters an eye from a luminous point outside is limited by the circular aperture of the iris. In an emmetropic eye the beam converges symmetrically to form a tiny pointlike image on the retina. Actually, this tiny image is a diffraction pattern, consisting of a relatively bright central disk (about 0.011 mm. in diameter) surrounded by several relatively dim concentric rings of rapidly diminishing brightness. For practical purposes, only the central disk need be considered.

In an astigmatic eye the beam of refracted light starts to converge toward a focus but not equally in all meridional planes.[1] Only in two planes, the principal planes, is an actual focus reached. The first focus is in the plane of the meridian of greatest curvature. The second focus is in the plane at right angles, the plane of the meridian of least curvature. The interval between the two focal planes is proportional to the amount of astigmatism.

The curvature of only the two principal planes is circular, or constant. In the intervening meridional planes it is elliptic.[2] No focus is reached in any of the intervening planes. The rays which enter through these planes do not remain in the same plane before and after refraction,[3] They run in directions which are skew to the optic axis and do not intersect the latter.

1. A meridional plane is one which passes through the normal to the corneal vertex, the optic axis.

2. Unlike the arc of a circle, the arc of an ellipse has a varying curvature. It is flattest where it meets the minor axis, and from there the curvature increases equally in both directions, to reach a maximum at the points of intersection with the major axis.

In an astigmatic eye the optic axis serves as a common minor axis for the elliptic refracting arcs of the innumerable meridional planes. Since, in a given medium, refracting power, or proximity of focus, is directly proportional to curvature, it is understandable that in the meridional planes refracting power increases with the distance along the elliptic arc from the optic axis.

3. The course of a plane beam of light, after refraction through the elliptic curve of an oblique meridional section of a spherocylindric refracting element, can be visualized with the aid of a projector and some converging lenses. Two strips of adhesive tape should be pasted across one surface of a cylindric lens so as to produce a very narrow slit oblique to the axis of the cylinder. Then, in combination with a spherical lens, the cylindric lens is fastened in front of a projector, the taped surface being nearest to the projector. A stenopaic slit may be placed next to the cylinder instead of the two strips of adhesive tape, if desired. Then a small circular beam of light is sent through the projector, and the light that emerges through the slit is studied by being intercepted at various distances with a small screen.

The oblique slit allows only a plane beam of incident light, rectilinear in cross section, to be refracted by the lenses. Immediately after refraction, the straight line, which represents the cross section of the narrow beam, starts to rotate along and about the optic axis. Simultaneously, the line starts rather rapidly to decrease in length. A minimum length, which is only a fraction of the length of the slit, is reached after rotation of about 75 to 90 degrees has occurred. Thereafter, the beam widens out again and continues its rotation. The rotation ceases after a total angle of from 140 to 170 degrees has been covered. Then the beam remains at its final inclination while its width (cross sectional length) increases indefinitely.

By placing a very narrow strip of tape transversely across the slit at various places the location of each point in the slit through the refracted beam can be ascertained from the corresponding shadows. It will be observed that, as the beam rotates and changes in width, each point in the slit maintains the same

(Footnote continued on next page)

Thus, in an astigmatic eye rays converge to a focus on the optic axis [4] in only two planes. These two principal planes always are at right angles to each other. A focal line which is perpendicular to the optic axis runs in each principal plane through the focal point of the other plane. The rays that enter in meridional planes other than the two principal planes pass through the two focal lines but do so away from the optic axis, which they do not intersect.

This varying refraction for different planes of incidence causes the initially circular beam of light to undergo characteristic and successive changes of contour. At first the cross section of the refracted beam is bounded by a progressively narrowing ellipse with its major (longer) axis in the plane of the meridian of least curvature and its minor (shorter) axis in the plane of the meridian of greatest curvature. Both axes diminish at uniform rates, the minor axis doing so more rapidly than the major axis. When the minor axis has decreased to a point, the ellipse has narrowed to a line—the first focal line. This line lies in the plane of the meridian of least curvature and is perpendicular to the optic axis. Beyond the first focal line the pointlike minor axis starts to increase and does so at the same rate at which it previously

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relative position in the cross sectional line. This indicates that the refracted rays do not intersect the optic axis.

Even though the rays of the oblique sections do not intersect the optic axis, they must pass through the two focal lines. The rotation of the refracted beam must harmonize with the position of the two focal lines. Therefore, in order that all rays may pass through the first focal line, the initial direction of rotation in all oblique meridional planes is toward the plane of the meridian of least curvature. After the first focal line has been passed, all rotation continues, so that at the second focal line all rays will lie in the plane of the meridian of greatest curvature. The rotating beams reach their minimum widths at various points along the interval between the two focal lines. The final position of rotation is reached in each plane in the space beyond the second focal line but rather close to it. These positions can be verified by simply removing the tape from the slit and observing the location of the two focal lines.

A crude model of the surface generated by such elliptic refraction of a plane beam of light can be made by pushing a series of toothpicks of proportionate decreasing and increasing lengths through and along the length of a drinking straw. The straw represents the optic axis, and the toothpicks are inserted in directions that correspond with the observed positions of the cross sections of the refracted beam. It is difficult to describe the resulting surface. Roughly, it may be said to resemble a helicoidal surface. Consideration of this surface indicates that the individual rays, in order to maintain rectilinear paths, as demanded by the theory of light, must pursue directions that are skew to the optic axis. The rays all cross the optic axis obliquely, but they are separated from it by varying intervals, and they do not actually intersect it.

4. The optic axis is not identical with the visual axis in the eye. An angle of about 5 degrees separates them at the nodal point. However, this slight separation does not materially impair the conclusions of this theoretic consideration.

decreased. The major axis, meanwhile, continues to shrink. When the two axes become equal in length, a circle is formed—the circle of least confusion. Beyond the circle the former minor axis becomes the major axis for the new series of elliptic cross sections and vice versa. Finally, a second focal line, perpendicular to the first, is formed in the plane of the meridian of greatest curvature. It passes through the focal point of the meridian of least curvature, perpendicular to the optic axis. Beyond the second focal line the beam continues to expand indefinitely in an elliptic contour with major axes in the plane of the meridian of greatest curvature.

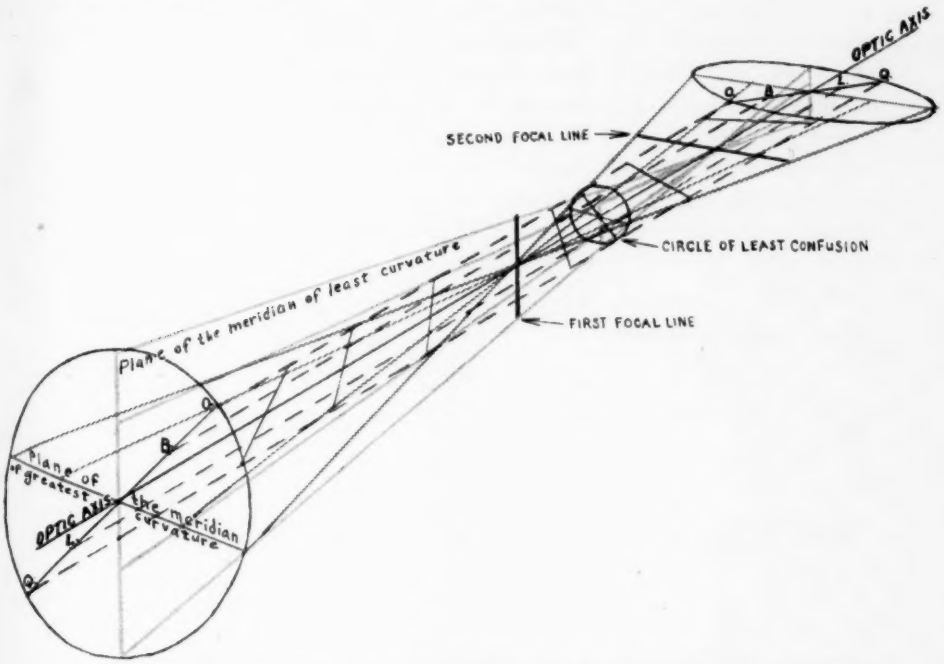

Fig. 1.—Schematic drawing which attempts to show the course of some of the individual light rays in Sturm's conoid. The course of the rays in an oblique meridional plane of incidence is particularly stressed. The paths of four rays (designated *O, B, L* and *Q*) which enter through such a plane are shown. They are depicted with interrupted lines in order to make it easier to follow their courses. Also, they are connected at various intervals by cross sectional lines, which indicate the progressive rotation that the original plane of incidence undergoes after refraction. The focal lines have been darkly shaded in order to indicate that they have a slight width.

The foregoing description of the contours of an astigmatic beam of light makes it evident that the image of an object point never can resemble a point. It must be, depending on the position of the retina, a diffusion pattern corresponding to an ellipse, a circle or a straight line.

The distances of the two focal lines behind the optical elements of an astigmatic eye vary inversely with the dioptric powers of the two

principal refracting meridians. The interval between the two lines, the interval of Sturm, depends on the amount of astigmatism—the difference between the dioptric powers of the two principal meridians.

THE FOCAL INTERVAL OF STURM

The whole bundle of refracted astigmatic rays is known as Sturm's conoid. As already mentioned, the part which lies between the two focal lines is called the focal interval of Sturm. Within this interval is the circle of least confusion. It is of interest to determine mathematically the location of this circle within the interval. This can be done with the aid of figure 2, which is a geometric representation of Sturm's interval. The two principal planes have been rotated about the optic axis so as to lie in the same plane. The following designations have been made in the figure: F_1 for the first focal point; F_2, for the second focal point; f_1, for the distance from the posterior principal plane of the eye to the first focal line; f_2, for the similar distance to the second focal line; a, for the length of the radius of the incident cylindric beam of light; c, for the radius of the circle of least confusion, and z, for the distance from the first focal line to the circle of least confusion.

From similar triangles

$$\frac{c}{a} = \frac{z}{f_1}$$

and

$$\frac{c}{a} = \frac{f_2 - f_1 - z}{f_2}$$

Therefore

$$\frac{z}{f_2 - f_1 - z} = \frac{f_1}{f_2} \tag{1}$$

or

$$z = \frac{f_1 (f_2 - f_1)}{f_1 + f_2} \tag{1 A}$$

It is evident from equation (1) that the circle of least confusion divides Sturm's interval into two lengths which are proportional to f_1 and f_2. Since f_2 always is numerically larger than f_1, the circle of least confusion cannot be midway between the two focal lines but must lie slightly nearer to F_1.

Since f_1 and f_2 represent the reciprocals of the posterior refracting powers of the two principal meridians, and since the latter, in turn, are proportional to the anterior refracting powers (the posterior refracting power multiplied by 1.336, the index of refraction of the vitreous, equals the anterior refracting power), f_1 and f_2 may be replaced in equation

(1) by $1/D_1$ and $1/D_2$, the latter symbols representing the anterior refracting powers of the two principal meridians. This changes equation (1) to

$$\frac{z}{f_2 - f_1 - z} = \frac{D_2}{D_1} \qquad (1\,B)$$

According to Gullstrand, the anterior refracting power of the eye varies from 58.64 D., with the accommodation relaxed, to 70.57 D., in maximum accommodation. Ordinarily, astigmatism of more than 4 D. is unusual, while astigmatism of more than 6 D. is rare. By substituting values in equation (1 B) which cover a range of refracting powers from as low as 50 D. to as high as 80 D. and a range of amounts of astigmatism from 1 to 6 D. it can be seen that the ratio $\frac{z}{f_2 - f_1 - z}$ varies from $\frac{1.0}{1.01}$ to $\frac{1.0}{1.1}$. Thus, although the circle of least confusion actually lies closer to the first focal line than to the second, for all practical purposes it may be regarded as lying midway between the two focal lines in the astigmatic eye. Even with 6 D. of astigmatism in an eye with minimal refractive power the forward displacement of the circle from the midposition corresponds to hardly more than ¼ D. of refractive power.

An equation for the size of the circle of least confusion also is easily obtained from figure 2.

Since

$$\frac{c}{a} = \frac{z}{f_1}$$

and

$$z = \frac{f_1\,(f_2 - f_1)}{f_1 + f_2}$$

$$\frac{c}{a} = \frac{f_2 - f_1}{f_1 + f_2}$$

or

$$c = \frac{a\,(f_2 - f_1)}{f_1 + f_2} \qquad (2)$$

It is apparent from equation (2) that the size of the circle of least confusion is proportional to the size of the radius of the incident beam of light or, what amounts to the same thing, to the diameter of the pupil of the eye. When the pupil is small, the circle is small. Also, the smaller the amount of astigmatism, the smaller will be the circle of least confusion.

PRACTICAL APPLICATIONS

The desideratum in the correction of astigmatism is a twofold one —the elimination of the interval of Sturm by making the two focal points of the principal meridians coincide and the displacement of the

resultant nonastigmatic image on the retina. However, many persons with astigmatism will not tolerate an immediate full correction. The resulting unequal prismatic distortions and displacements of objects are too annoying. In cases of this kind the oculist should strive to

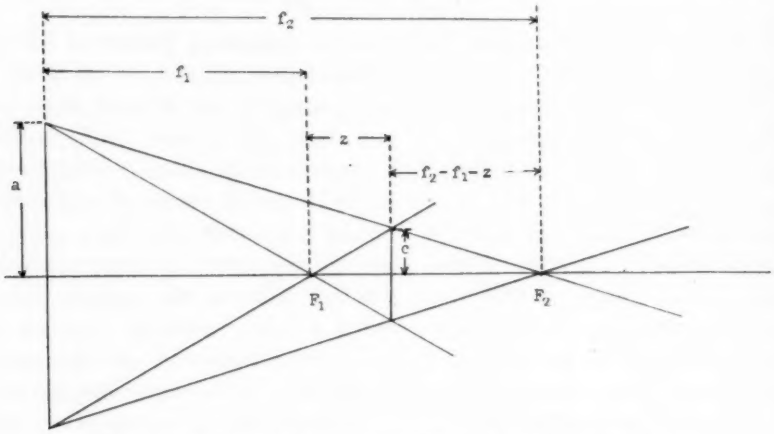

Fig. 2.—A geometric representation of Sturm's conoid.

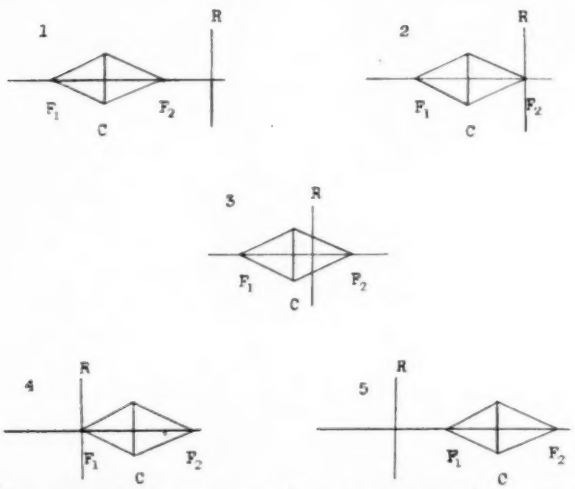

Fig. 3.—Diagram illustrating the position of the focal lines (F_1 and F_2) and the circle of least confusion (C) with respect to the retina in the various astigmatic conditions. *1* shows the positions in compound myopic astigmatism; *2*, in simple myopic astigmatism; *3*, in mixed astigmatism; *4*, in simple hypermetropic astigmatism, and *5*, in compound hypermetropic astigmatism.

do two things. First, he should reduce the interval of Sturm, and with it the size of the circle of least confusion, by a partial correction of the cylindric error. Then, with spherical correction, he should shift the position of the reduced astigmatic interval so as to bring the

circle of least confusion on the retina. In the absence of a full correction it is believed that an astigmatic eye will have its clearest and most comfortable vision whenever the circle of least confusion coincides with the retina.

The position of the two focal lines relative to the position of the retina is revealed by refraction. These lines can be shifted by means of spectacle lenses. A converging lens moves images forward, and a diverging lens displaces them backward. Spheres affect all meridians equally and will shift F_1 and F_2 through equal intervals. Cylinders exert a maximum effect in the meridian at right angles to the axis and have no effect in the meridian parallel to the axis. Correctly placed, a cylinder will shift the position of only one of the two focal lines—the one that is farther from the retina—and will not change the location of the other.

In those cases in which only a partial correction of the astigmatism seems advisable there must be added to the partial cylindric correction a spherical correction sufficient to move the circle of least confusion on to the retina. The amount of spherical power that is required is half the dioptric value of the remaining uncorrected astigmatism (the circle of least confusion is approximately in the middle of the focal interval) plus the dioptric value of the distance between the retina and the nearer focal line (the second focal line in the myopic eye and the first focal line in the hypermetropic eye). In cases of hypermetropia the spherical power thus calculated must be decreased by an allowance for the accommodative tonus. Two examples will illustrate this rule. If the full correction is — 3.00 D. sph. ⊂ — 5.00 D. cyl. and it is desired to correct only half the astigmatism, the prescription should read — 4.25 D. sph. ⊂ — 2.50 D. cyl. In the second case, if the total correction is + 6.00 D. sph. ⊂ + 4.00 D. cyl. and it is deemed advisable to correct only 2.50 D. of the astigmatism, the prescription should read + 6.75 D. sph. ⊂ + 2.50 D. cyl. less whatever spherical allowance is made for the strength of the ciliary muscle.

A similar procedure was recommended by Copeland,[5] who arrived at his conclusions by an obscure graphic method. Copeland stated:

> . . . if the cylinder is reduced a change must be made in the spherical element of the lens. . . . In reducing the cylindric element of any correction add half of the amount of the reduction to the sphere, maintaining the sign of the cylinder in the addition.

Copeland also introduced the term "spherical equivalent of the compound" for the spherical combination of half the dioptric value of the astigmatic correction plus the spherical correction.

30 East Fortieth Street.

5. Copeland, J.: An Official Study in the Application of Cylindric Corrections, Optom. Weekly **19**:191 (April 5) 1928.

SIGNIFICANCE OF ANISEIKONIA IN AVIATION

WING COMMANDER A. J. ELLIOT
ROYAL CANADIAN AIR FORCE

THE word "aniseikonia" is derived from the Greek roots *ἄνισος* and *εἰκών* meaning literally "unequal image." It may be defined as that condition of the binocular visual apparatus in which the ocular images as seen by the two eyes are unequal in either size or shape or in both. The term ocular image does not refer to the retinal image, but it is applied to the final impression which reaches consciousness in the higher brain centers.

Aniseikonia is of two principal types: (1) over-all difference, in which one image is larger than the other in all meridians, and (2) meridional difference, in which one image is larger than the other in one meridian. Combinations of the two forms may occur. If the ocular images are markedly unequal in size and shape, there may be a disturbance of binocular vision, which may or may not be apparent to the patient.

ANISEIKONIA AND FLYING PERFORMANCE

The significance of aniseikonia in flying performance has been a matter for conjecture since 1935, when Ames [1] first called attention to this aspect of the subject. He aroused interest concerning the importance of aniseikonia in the perception of depth among investigators in the field of aviation medicine. In addition, Ames and his associates showed that aniseikonia affects stereoscopic vision, and he suggested, therefore, that the anomalous spatial localization resulting might interfere with the pilot's judgment of distance. Since that time the literature on aviation medicine has contained frequent reference to the possible correlation of flying performance and the presence of aniseikonia. Noteworthy among those who have discussed this subject is Armstrong,[2] who in his textbook states "that aniseikonia affects stereoscopic vision

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Read at a meeting of the Canadian Ophthalmological Society, Montreal, Canada, Sept. 21, 1942.

This paper is a résumé, with added references, of a report submitted to the Associate Committee on Aviation Medical Research, National Research Council of Canada, July 12, 1942.

1. Ames, A., Jr.: Aniseikonia—A Factor in the Functioning of Vision, Am. J. Ophth. **18**:1014, 1935.

2. Armstrong, H. G.: Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1943.

and may interfere with the pilot's judgment of distance and may make it impossible for him to correctly estimate the true position of the plane of the earth below him."

It was considered important in the Royal Canadian Air Force to evaluate the significance of aniseikonia in its practical relationship to flying, for three reasons: (1) aniseikonia may interfere with stereoscopic vision, as just stated; (2) the presence or absence of aniseikonia is not determined by the routine ophthalmic examination, and (3) there were numerous pilot trainees who had ceased training because of inability to land an aircraft successfully.

SELECTION OF CANDIDATES FOR EXAMINATION FOR ANISEIKONIA

The study of the relationship of aniseikonia to flying performance was limited to its correlation with the ability of the airman to land an aircraft successfully. To this end, a selected group of 175 pilots who had ceased training was examined for the presence and amount of aniseikonia. Also, a control group of 50 experienced pilots, all of whom were instructors, was studied.

The 175 airmen were trainees who had ceased training because of one or more experiences with difficulties in landing most important among which was incorrect judgment of height and distance in landing the plane. The majority of the airmen examined for aniseikonia had ceased training during the period between the tenth and the fifteenth hour of their flying training. In the case of a minority the poor landings were manifested with the faster and heavier aircraft after approximately one hundred flying hours, at which time they were forced to cease training.

A suitable form outlining the most important landing errors was utilized at the flying schools in the cases of the airmen who had ceased training because of landing difficulties. The form was completed by the medical officer at the flying school, with the assistance of the airman's instructor. In addition to landing errors, which were directly attributable to faulty judgment of height and distance, other factors, such as air speed, coordination and nervousness, were included in the table. All types of landing errors were noted even though one or more of the errors might occur during a landing as a result of defective judgment of height and distance. In this way it was possible to correlate the landing difficulties of the airmen with the data on aniseikonia, obtained later.

A control group of 50 experienced pilots was examined for whom the judgment of height and distance was considered to be satisfactory by virtue of their satisfactory landing performance. The amount of aniseikonia was determined for each of the experienced pilots.

ROUTINE EXAMINATION OF THE EYES

In each case, before the examination for aniseikonia was performed, it was necessary to have general information concerning the condition of the eyes of the airmen or pilot. A suitable form was used for the study, which included the data obtained in the routine ophthalmic examination and in the examination for aniseikonia. The routine ophthalmic examination was similar to that employed in the categorization of aircrews in the Royal Canadian Air Force. This included the assessment of the visual acuity at 20 feet (6 meters) using the Project-O-

Chart, and determination of whether or not the manifest hypermetropia exceeded 2.50. The extraocular muscle-balance at 6 meters and at 25 cm. was determined by means of the Maddox rod and cover tests. The accommodation in each eye and the objective convergence were ascertained. When indicated, a manifest or cycloplegic refraction was performed.

APPARATUS USED IN MEASUREMENT OF ANISEIKONIA

The examination for aniseikonia was performed with the space eikonometer developed by the Dartmouth Eye Institute. The space eikonometer measures aniseikonia at any axis, in addition to axis 90 and axis 180, and hence it gives direct information as to the nature of a subject's spatial localization. The "leaf room" was also used in additional corroboration of the measurements with the space eikonometer.

CORRELATION OF ANISEIKONIA AND PERFORMANCE FOR 175 PILOTS WHO HAD CEASED TRAINING AND FOR 50 EXPERIENCED PILOTS

In order to interpret the data obtained from the examination for aniseikonia of the 175 pilots who had ceased training and the 50 experienced pilots, it was necessary to correlate the flying performance with these results. The flying performances in landing were conveniently divided into four types: The pilots who had ceased training consistently leveled off too high or too low, or were erratic in landing and leveled off too high or too low at different times. These three types were compared with the performance of experienced pilots whose landing performance was known to be satisfactory. Of the 175 pilots who had ceased training, 48 per cent were found to have leveling off too high as their most important landing fault; 32.6 per cent consistently flew into the ground, and 19.4 per cent were erratic and committed each of the these landing faults at different times.

The amount of aniseikonia in the vertical meridian was less than 0.40 per cent in 76.6 per cent of the 175 pilots who had ceased training and in 82 per cent of the 50 experienced pilots (fig. 1*A*). In the remaining pilots with slightly greater amounts of aniseikonia in the vertical meridian, with which anomalous spatial localization might be expected to be rather pronounced, this degree of aniseikonia was not of practical significance in the landing of aircraft because of the importance of monocular visual clues.[3] No significant correlation with performance in landing was found to exist.

3. As a corollary of this study, it was noted that monocular visual clues assume an importance in the judgment of distance in landing aircraft which has not hitherto been sufficiently recognized. In the past it had been considered that this judgment was made by stereoscopic visual clues (a binocular function), and, while such monocular clues as perspective, shadow, overlay and size of retinal image

The aniseikonia in the horizontal meridian was less than 0.40 per cent in 86.4 per cent of the pilots who had ceased training and in 98 per cent of the experienced pilots (fig. 1 *B*). No significant correlation with landing performance was demonstrated.

These figures for aniseikonia are in remarkable agreement with the results of Peckham [4] in a study of 252 aviation cadets and instructors of the United States Navy. He found that 92 per cent of the subjects showed less than 0.50 per cent of aniseikonia.

The determinations of cyclophoria were important in that plus cyclophoria results in binocular visual clues appearing nearer and minus cyclophoria results in binocular visual clues appearing farther away.

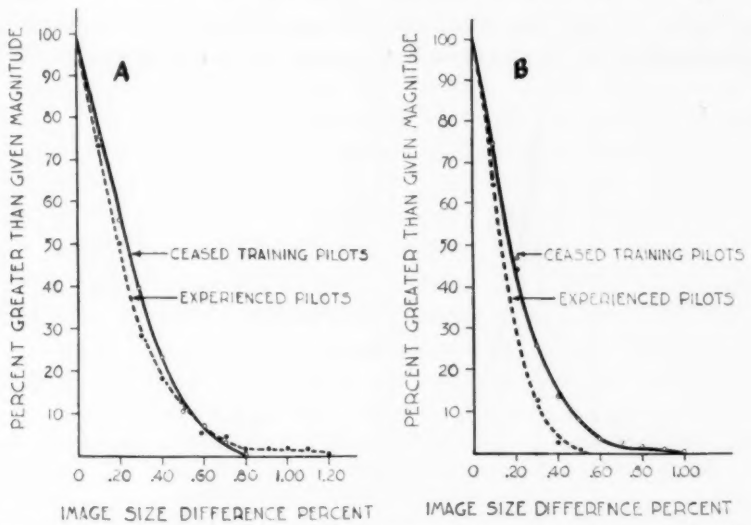

Fig. 1.—Aniseikonia (*A*) in the vertical meridian and (*B*) in the horizontal meridian in 175 pilots who had ceased training and in 50 experienced pilots.

The conclusion was reached that the values for cyclophoria proved to represent the normal distribution for a highly selected group of the population and that no practical relationship existed between landing performance and the presence of cyclophoria in the groups studied

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were recognized, they were not considered important in the total judgment which the pilot makes in the landing of the aircraft.

Since aniseikonia is a binocular dysfunction, the anomalous spatial clues must be significantly great to overshadow the important monocular clues. In the vast majority of situations in aviation, monocular clues predominate in landing fields both by day and by night, and only in the unusual case do stereoscopic visual clues overshadow the monocular clues.

4. Peckham, R. H., in discussion on Lancaster, W. B.: Nature, Scope and Significance of Aniseikonia, Arch. Ophth. **28**:767 (Nov.) 1942.

(fig. 2). Peckham [4] studied the space perception in his subjects by means of their response with aniseikonia lenses to a frontal plane set before them. He felt that there was a significant difference between the two groups on this apparatus.

No significant correlation was noted between landing performance and the standard deviation of the settings on the space eikonometer.

It was shown that no relationship existed between landing performance and the presence of base-out asymmetry lenses or base-in asymmetry lenses.

EFFECT OF ANISEIKONIA LENSES ON ABILITY TO LAND AIRCRAFT

A series of landings were made in aircraft in order to study the practical effect of various aniseikonia lenses on the judgment of height

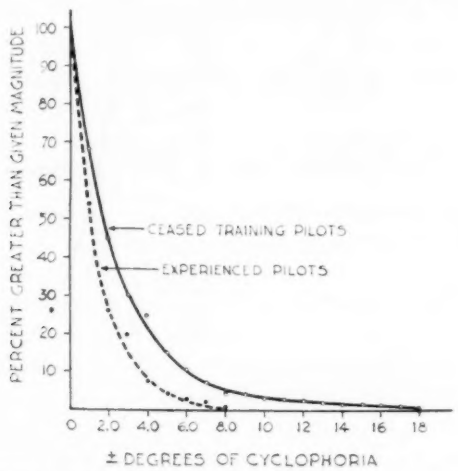

Fig. 2.—Cyclophoric aniseikonia in 175 pilots who had ceased training and in 50 experienced pilots.

and distance. The landings were made in a twin engine service trainer airplane. In this aircraft the pilot and co-pilot were seated side by side, and I was immediately behind the pilots. An excellent view in all directions was available both to the pilot and to me, so that I had as good a view of the landing field as the pilot.

A wide selection of aniseikonia lenses was used for this aspect of the study. They included 1, 2 and 4 per cent aniseikonia lenses at axes 45, 90, 135 and 180, in various combinations. The lenses were worn in the aircraft by the co-pilot and by me during the take-off, flight and landing.

The most pronounced effects on the judgment of height and distance produced by wearing aniseikonia lenses were present while we were

landing on a level grass field at some distance from its boundaries, and where no parked aircraft were present. In this situation binocular visual clues are almost the only ones present, and the anomalous spatial localization has a marked effect. When the co-pilot was attempting a landing on this field and was wearing a 1 per cent aniseikonia lens at axis 45 in front of the right eye and at axis 135 in front of the left eye, there was a tendency for him to level off the aircraft too soon, at about 30 or 40 feet (9 or 12 meters) above the ground. When the co-pilot was wearing a 1 per cent aniseikonia lens at axis 135 before the right eye and at axis 45 before the left eye the ground appeared farther away than it actually was, and he had a tendency to fly into the ground. A 1 per cent aniseikonia lens at axis 45 before the right eye and another at axis 135 before the left eye is equivalent to a measurement of + 15 on the space eikonometer. A 1 per cent aniseikonia lens at axis 135 before the right eye and another at axis 45 before the left eye is equivalent to a measurement of — 15 on the space eikonometer. In this study there were only 2 pilots who had ceased training for whom readings of ± 15 were obtained on the space eikonometer. Less marked changes in the apparent distance above the ground occurred when the pilot landed while wearing the various other aniseikonia lenses.

When the co-pilot landed the aircraft on an improved paved runway while wearing 1 per cent aniseikonia lenses at axis 45 in front of the right eye and at axis 135 in front of the left eye, or the reverse, the errors in the judgment of height were almost nil. This airdrome was of the standard type, with many crossed runways, hangars and nearby parked aircraft. Here the important monocular visual clues overshadow the anomalous spatial clues produced by wearing aniseikonia lenses. The judgment of distance in this situation is based largely on the monocular visual clues. In this situation the co-pilot made successful landings while wearing the aniseikonia lenses mentioned.

Neither the co-pilot nor I made any remarkable observations during takeoffs or in flight while wearing the various aniseikonia lenses.

It can be concluded that in the landing of aircraft the presence of 1 per cent aniseikonia lenses at axis 45 and at axis 135 in front of the eyes in either combination has a definite effect on the judgment of distance when predominantly binocular visual clues are present. However, the same lenses have little effect on the judgment of height when monocular visual clues predominate.

CONCLUSION

The relationship of aniseikonia to flying performance in landing of aircraft was investigated in two selected groups. In the first group

there were 175 trainees who had ceased training because of difficulties in landing and in the second group there were 50 experienced pilots.

The amounts of aniseikonia were found to be very small, and no practical correlation with landing performance could be ascertained in the groups studied.

A series of landings were made in aircraft in order to study the practical effect of various aniseikonic lenses on flying performance during landing. It was noted that when monocular visual clues predominated, as was usually the case, the flying performance was not affected by the anomalous binocular clues produced by wearing aniseikonic lenses.

170 St. George Street, Toronto, Canada.

MEDICAL TREATMENT OF ACUTE GLAUCOMA

MANUEL JOSÉ ICAZA, M.D.
MEXICO, D. F., MEXICO

It is certainly a curious, but explicable, fact that by living constantly in the presence of a difficulty man becomes less apt to overcome it.—*Prof. Dr. Charles Nicolle.*[1]

SELDOM do oculists encounter in the exercise of their profession a more dramatic scene than that of an acute attack of glaucoma.

Within a few minutes, sometimes quite suddenly, the patient is stricken with violent pain in one eye, pain which radiates toward the ear, teeth and all over the head and may reach an intolerable pitch. He loses sleep and appetite and frequently is subject to nausea, or even vomiting, and fever. Sometimes, owing to the intensity of the pain, he loses consciousness. At the same time the visual power fails rapidly and in some cases disappears completely in a few hours. In other cases the patient perceives lights as though through fog and surrounded by rainbow-colored rings.

On examining the patient, one finds edema of the lids; there is a constant flow of tears; the conjunctiva is edematous, or even chemotic, and of a dark dusky red color; the cornea is turbid, like unpolished glass; the anterior chamber is shallower than normal; the iris is discolored and narrowed and almost in actual contact with the cornea; the pupil, dilated, oval and eccentrically situated, has taken a grayish green color. On touching the eye, one finds it hard as a marble and terribly painful.

In the presence of this acute attack of glaucoma, knowing that the only remedy available is that of operation, and in spite of the gravity of the symptoms, one has to wait until the eye is brought to such a condition that it can be operated on. Meanwhile, miotics and analgesics are applied. But the patient continues to complain of horrible pain, impossible to bear, which is not relieved by any known analgesic, not even morphine; and the visual power gradually diminishes.

This condition may last for several days—the dreadful pain, driving the patient to the brink of madness, and the hardening of the eye to the point of blindness—until, at long last, the oculist can operate—always under extremely difficult conditions and always running the great risk of hemorrhage by thorough sudden decompression. And often the operation has been too late to save the eye.

1. Cited by Un Asclepióde, Clínica, Barcelona **12**:127, 1935.

All of us oculists have seen and suffered in the face of such cases, which always leave with us a bitter taste of our own impotence.

TECHNIC OF RETROBULBAR ANESTHESIA

In 1914 Pooley [2] extended to all ophthalmic surgery the anesthetic maneuver used before only for enucleations and eviscerations, by Siegrist [3] (1907) and by Elschnig [4] and Löwenstein [5] (1908), thus completing the anesthetic technic for operations on the eye. This measure consisted in injecting the anesthetic solution into the apex of the orbit, infiltrating the retrobulbar tissues and, by blocking all the sensory nerves of the eye—the long ciliary nerves, efferent branches of the ciliary ganglion, and the short ciliary nerves, branches of the nasal nerve—obtaining their functional section. This maneuver rendered painless each step of all ophthalmic operations and was immediately accepted the world over. It can be said of every oculist that to know the method was to adopt it immediately. Since then, the retrobulbar injection of an anesthetic has become a necessary preliminary step to almost every operation on the eye.

Among ourselves, ophthalmologists in Mexico, I cannot state who was the first to use it, or when; but I have enough information to be able to state that in 1918 it was in everyday use in the Hospital de Nuestra Señora de la Luz, which was the first institution in Mexico to adopt this form of anesthesia. (In his thesis, Palacios Macedo,[6] refers to the technic used in this hospital, which I myself described to him at the time he was writing the thesis, in 1918.) The anesthetic solution in use now, and for many years, in the Hospital de Nuestra Señora de la Luz is as follows:

Distilled, boiled water	100 cc.
Procaine hydrochloride	2.00 Gm.
Sodium chloride	0.50 Gm.

(in sterilized vials)

If necessary, 0.1 cc. of a 1:1,000 solution of epinephrine hydrochloride is added to each cubic centimeter immediately before using. This quantity (1 cc.) is the amount used for the retrobulbar injection of the anesthetic.

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2. Pooley, G. H.: Improvement in Local Anaesthesia in Operations upon the Eyes, Opthalmoscope **12**:464-467, 1914.

3. Siegrist, A.: Lokalanästhesie bei Exenteratio und Enucleatio bulbi, Klin. Monatsbl. f. Augenh. **45**:106-109, 1907.

4. Elschnig, A.: Hilfsverfahren bei der Altersstarektrakion, Arch. f. Augenh. **98**:300-305, 1927.

5. Löwenstein, A.: Ueber regionäre Anästhesie in der Orbita, Klin. Monatsbl. f. Augenh. **46**:592-601, 1908.

6. Palacios Macedo, J.: Local and Regional Anaesthesia in Head and Face Operations, Thesis, Mexico City, Universidad Nacional de México, 1919.

In using this injection, my colleagues and I were all able to observe the following results: complete anesthesia of the ocular globe and its annexa, rapid and complete dilation of the pupil and noticeable lessening of the intraocular tension. Sometimes, indeed, the eye becomes softer than desired, for many operations, such as the incision for cataract operation, are made more difficult by too great a softening of the eye. On occasions this softening may even cause complete corneal collapse. Day by day we saw all this and were most familiar with all these effects. But none of us associated the action of the drug with the relief of acute glaucoma.

APPLICATION TO TREATMENT OF ACUTE GLAUCOMA

Once, when I was confronted with a difficult operation on an exceedingly softened eye, I found myself thinking: "If this injection removes the pain and softens the eye to such a degree, it must be the rational treatment for an acute attack of glaucoma."

Afterward, in my mind the thought persisted: "The constant pupillary dilatation adds to the obstruction of the iridocorneal angle, the straining angle, and may thus be harmful to the eye in a case of glaucoma." "Why is the pupil dilated, and why, at the same time, is the ocular tension lessened?"

The German Bayer's Novocain and the American Abbott's procaine, in themselves chemically identical (β-diethylaminoethyl-p-aminobenzoate hydrochloride), are synthetic cocaine substitutes, much less toxic than cocaine and with no action on the sympathetic nerve to the iris. These agents are not likely to cause pupillary dilation or softening of the eye.

Epinephrine is, of course, a stimulant of the sympathetic nerve. But the quantity (0.0001 Gm.) which we inject in a cubic centimeter of our anesthetic solution and the place where it is injected minimize its direct action on the dilatory muscles of the pupil. On the other hand, the amount is sufficient to produce a strong constriction of the ciliary vessels, by contact, on infiltration of the retrobulbar tissues. This action of epinephrine on the eyes, fully described by Darier,[7] according to the experiences of Zimmermann, Wessely, Lewandowsky, Darier and others, is exerted directly on the walls of the vessels, and the anemia which results from the constriction of the vessels of the iris and ciliary body always causes the lessening of ocular tension and produces the dilatation of the pupil by diminishing the volume of the iris and the ciliary body. Grandclément,[8] of Lyons, affirmed that instillation of epinephrine might be a

7. Darier, A.: Leçons de therapeutique oculaire faites à la Faculté de Médecine de Paris, Paris, Bureau de la clinique ophtalmologique, 1901, pp. 120-128.

8. Grandclément, cited by Darier, A.: Traité complet de thérapeutique oculaire, ed. 2, Paris, Jouve et Cie, 1923, p. 283.

good treatment for inflammatory glaucoma. It has been usual (as recommended by all the great oculists) to add epinephrine to miotic collyriums, the action of which it tends to increase.

Thinking over all this, I became convinced that I had found, theoretically, the ideal treatment for an acute attack of glaucoma.

To prevent pupillary dilation and to lengthen the effects of the retrobulbar injection, I instilled before and after the injection, taking advantage of the anemia of the eye, a 1 per cent solution of pilocarpine nitrate and a 0.5 per cent solution of physostigmine salicylate; from the very first time I tried to realize my idea, and I was gratified with magnificent results.

In November 1941 I presented a report of my efforts before the Ophthalmological Society of the Hospital de Nuestra Señora de la Luz, and this study was published in the hospital's bulletin of the same month.[9] The results of my first experiences could not have been more encouraging.

This procedure has been, since then, in constant practice in this hospital in every case of acute glaucoma. More than 200 patients have been successfully treated with the retrobulbar injection of 1 cc. of a 2 per cent solution of procaine hydrochloride with the addition of epinephrine hydrochloride (0.0001 Gm. per cubic centimeter), always preceded and followed by instillations of pilocarpine and physostigmine. In our hospital, this method has become a matter of routine, and invariably produces the same results: In a few minutes (in 1 case in only six minutes) the pain disappears completely, and we also note the rapid and complete disappearance of all signs of ocular hypertension; that is, the opacity of the cornea, caused by edema, clears, the pupil contracts strongly under the effect of the miotics, the conjunctiva acquires a pale (normal) color, the eye softens and, when this is still possible, the visual power improves and the field of vision is enlarged. These eyes have been operated on, days or weeks later, under perfect conditions of tension for the operation, and without the patient having suffered a recurrence of the pain.

The following year, in 1942, Levitt[10] published an article on the practical treatment of glaucoma, in which he referred to the retrobulbar injection of procaine, alone or with mecholylchloride, as a means of relieving ocular tension and so of obtaining better conditions under which to operate. In the résumé of his work that I have read, it is not specified whether he uses the injection as a preoperative step only. I do not know, therefore, whether he and I are in agreement

9. Icaza, M. J.: Un paliativo util en el glaucoma agudo, Bol. d. Hosp. oftal. dc Ntra. Sra. de la Luz **1**:258-260, 1941.

10. Levitt, J. M.: Practical Management of Primary Glaucoma, Dis. Eye, Ear, Nose & Throat **2**:249-251, 1942.

as to its use, aside from the operative technic. In any case, Levitt's article was written and published in August 1942, nine months after mine, of November 1941.

COMMENT

Of course I do not believe that this treatment is the remedy for glaucoma. But I am convinced that it is the most useful pálliative measure yet found, with which one is able first to give the patient complete relief from great pain and, second, to put the eye in such condition as to permit the surgeon to choose without haste the treatment which he may judge most adequate in each case and to apply it at exactly the right time, without danger of complications.

I do not pretend to be the initiator of the retrobulbar injection, which has been known and used for a long time. But it had been always employed only as a preliminary step to the operation, as a part of the anesthetic technic. To the best of my knowledge, I was the first to use it as a method of treatment in itself, applied at the very moment of an acute attack of glaucoma.

Considering that it may prove of practical utility, I have decided to publish my experiences with this treatment, in the hope that oculists who may do me the favor of reading about them may find a simple and harmless method, available at any moment, which they may use repeatedly if necessary (I have not yet needed to repeat the injection) to fulfil the two most urgent needs in an acute attack of glaucoma, namely, the deadening of the pain and the lessening of the ocular tension; alleviating in this way the patient's unbearable pain and, at the same time, conditioning the eye to receive definite surgical treatment.

CATARACT ASSOCIATED WITH INTRAOCULAR TUMORS

BERNARD SAMUELS, M.D.
NEW YORK

IN FOUR previous papers, I [1] described the microscopic observations in cataracts associated with ulcers of the cornea,[1a] scars of the cornea,[1b] spontaneous iritis [1c] and detachment of the retina [1d] and traced the causes of these cataracts. The present paper, the fifth of the series, concerns cataracts which develop in the course of intraocular tumors.

Fortunately, in most cases the lens is not affected by the tumor in the preglaucomatous stage, and the examination of the fundus is unhindered. However, it may happen in the early stages of a tumor that a mistaken diagnosis of incipient cataract is made because the changes in the lens would seem to be enough to explain the visual disturbance. In the glaucomatous stage a combination of cataract, iridocyclitis and glaucoma may present a picture so complicated that a tumor would not be suspected as the underlying cause.

In the routine of clinics, a special cause of diagnostic error in a case of a tumor concealed by a cataract is failure to obtain a complete history. In response to ordinary questioning a patient is apt to give symptoms similar to those elicited in a case of detachment of the retina, because a tumor of the choroid may cause but slight visual disturbance prior to the detachment of the retina. It is only by putting direct questions to a patient that he can be made to recall that the earliest sign of disturbance of vision was a distortion of objects, or an impression of dark waves before the eye, or a sensitiveness to light in a certain quadrant, or dizziness. Often it is not until the globe is inflamed and painful that the patient consults the oculist.

MATERIAL

The material for the present paper consisted of microscopic preparations from 57 globes, each containing an intraocular tumor. In 34 globes the tumor was a malignant melanoma and in 21 globes a retinoblastoma. In 1 globe there was an

Read at the Eighty-First Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., Nov. 11, 1945.

1. Samuels, B.: (*a*) Lesions in the Lens Caused by Purulent Corneal Ulcers, Tr. Am. Ophth. Soc. **39**:66-72, 1941; (*b*) Cataract Complicating Corneal Scars After Perforating Ulcers, ibid. **40**:292-304, 1942; (*c*) Pathology of the Lens in Non-Traumatic Iritis, ibid. **41**:262-272, 1943; (*d*) Complicated Cataract Associated with Spontaneous Detachment of the Retina, ibid. **42**:109-117, 1944.

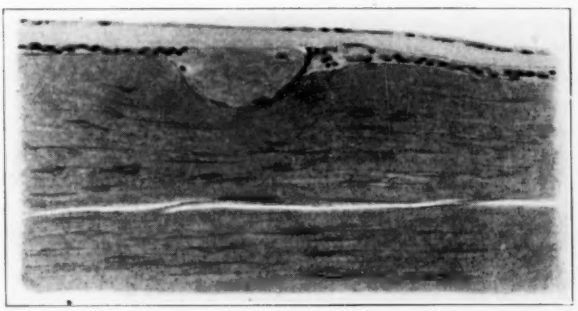

Fig. 1.—Detachment of subcapsular epithelium by a druse in a case of malignant melanoma of the choroid in the globe of a girl aged 17 years. The drawing is of a section from the pupillary area. The subcapsular epithelium is detached by a hemispherical mass resembling the capsule of the lens in staining reaction, although it lacks its uniform quality. At its base the epithelium exhibits some proliferation. A few fibroblasts are scattered over the anterior surface of the capsule.

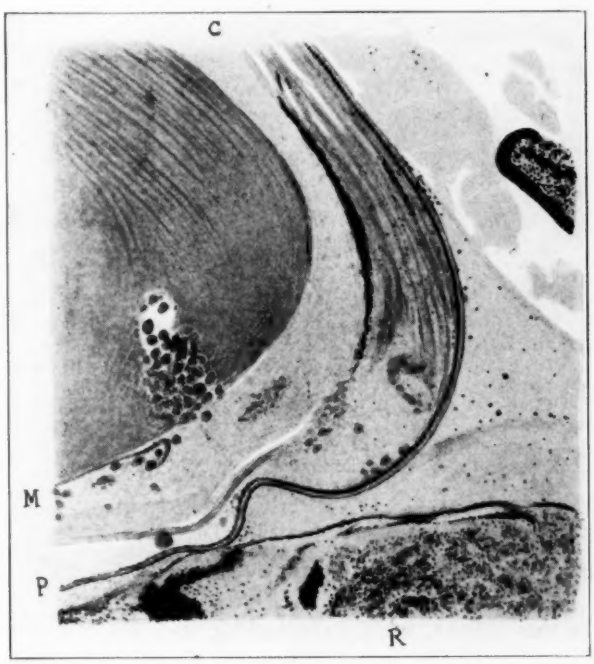

Fig. 2.—Morgagnian globules and calcification in a case of retinoblastoma. The nucleus of the lens is more darkly stained than the cortex (*C*). Capping the equator is a thin crust of chalk. Posteriorly, at *P*, the lenticular cells are disintegrating. A number of morgagnian globules (*M*) are present in the cortex, and a group of them are in the nucleus. The degenerated retina (*P*) is in contact with the lens.

epithelioma of the ciliary body and in another a sarcoma that invaded the ciliary body from the limbus. Considering how long a lens may remain unaffected in a case of intraocular tumor, the material is indeed a large one.

In the course of this paper it will be brought out that the tumor was not in every instance the actual sole cause of the cataract. Complications that developed in the globe during the growth of the tumor or during its degenerative change were either the direct or the contributing factor in formation of some of the cataracts. It suffices to say here that of the 57 tumors 26 were in contact with the lens. Seventeen of the melanomas were necrotic; 12 were almost entirely so, and all the retinoblastomas showed signs of necrosis.

PATHOLOGIC DETAILS

1. *Folds in the Capsule.*—In a discussion of anatomic details, folds of the capsule deserve to come first, because they are among the most conspicuous of all the changes to which the lens is ordinarily subjected.

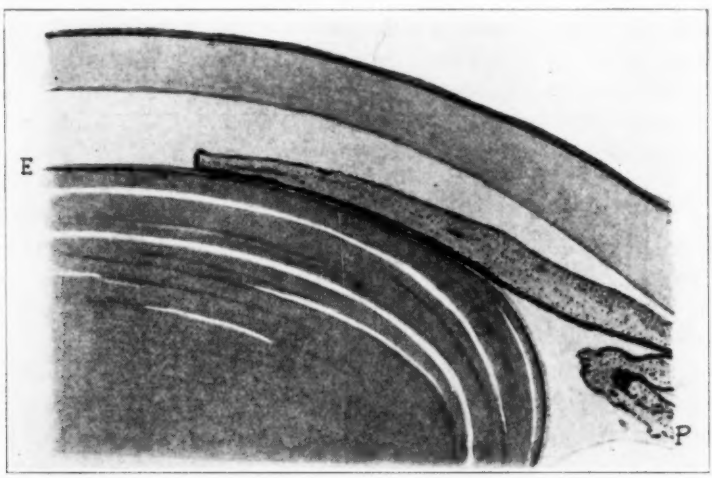

Fig. 3.—Necrosis of epithelium under a necrotic pupillary zone in a case of malignant melanoma of the choroid in a globe of a woman aged 40 years. The lens was pressed forward by the detached retina. The epithelium of the lens (*E*) is normal in the pupillary opening and at the equator. Between these two areas, exactly where the necrotic iris comes in contact with the lens, there is a stretch in which the epithelium has disappeared. The sphincter muscle is gone, as are the chromatophores in the stroma to a great extent. The ciliary processes are necrotic, and their pigment layer is dispersed. The anterior chamber is shallow, and the filtration angle is blocked.

However, in this survey, folds were lacking in a majority of the cases. In the cases of retinoblastoma folds were found but once, and then in connection with a large anterior polar cataract that threw the overlying capsule into numerous ruffles. The tumor was surprisingly small and showed but little necrosis. The iris was greatly inflamed. Iritis is rarely present in cases of retinoblastoma, although early necrosis is a characteristic of this tumor. In this case it was not believed that

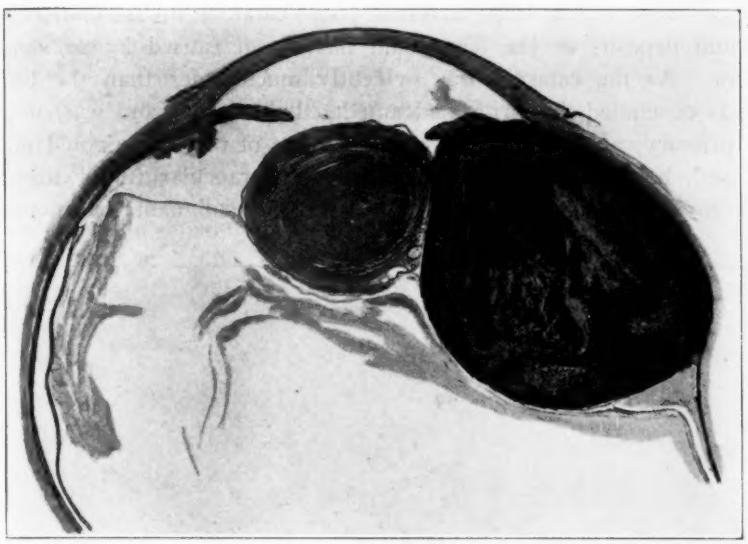

Fig. 4.—Absorption of lens at the equator and posterior cortical cataract. A malignant melanoma of the ciliary body produced iridodialysis. The lens is in its normal position. The substance, and not the epithelium and capsule, has vanished in the area pressed on by the tumor. The anteroposterior diameter of the lens is increased. The capsule is thrown into folds at the posterior angle between the lens and the tumor, and in the adjoining cortex there are large cystic spaces.

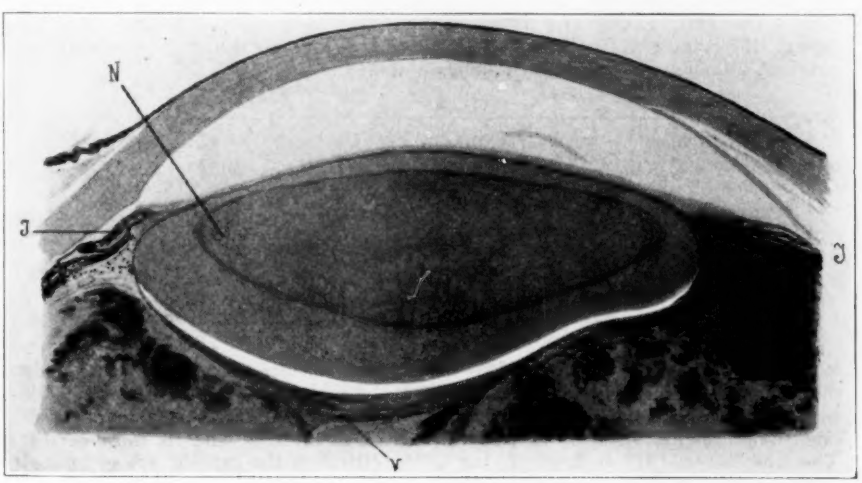

Fig. 5.—Morgagnian cataract in a case of retinoblastoma in a globe of a girl 1 year of age. The iris (*I*) was so shrunken that the pupil was of maximum width. In the lens, a faintly staining nucleus (*N*) is visible in a fluid cortical material, which is broader at the posterior pole. At the equator of the nucleus (*N*) there are a number of cellular elements—the remains of the germinal zone. The anterior subcapsular epithelium is in order. It disappears just behind the equator. The vitreous (*V*) lies compressed between the necrotic tumor and the lens. In spite of the child's age a nucleus is present; otherwise there would have been total liquefaction.

intense iritis and a large anterior polar cataract in association with calcium deposits in the lens could have been caused by so small a tumor. As the cataract was evidently much older than the tumor, it was concluded that iritis had antedated the tumor and was, in fact, the primary cause of the cataract. The age of the tumor could not be guessed, because in exceptional cases an intraocular tumor may not enlarge for years. Among the cases of malignant melanoma of

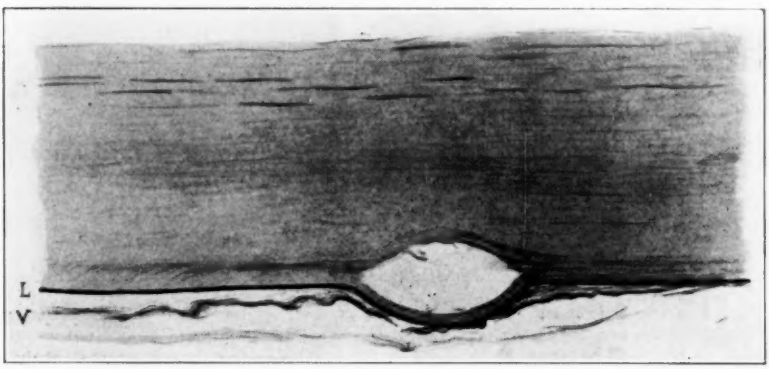

Fig. 6.—A curious cystic space in a case of retinoblastoma. Posteriorly a relatively large, oval cystic space is seen, filled with a slightly staining fluid. The substance of the lens separates it from its jagged walls, the posterior wall being thin. The lens capsule (*L*) is caused to bulge backward. The space has no lining. *V* represents the compressed vitreous. This formation is probably an artefact, although its fluid content takes a stain.

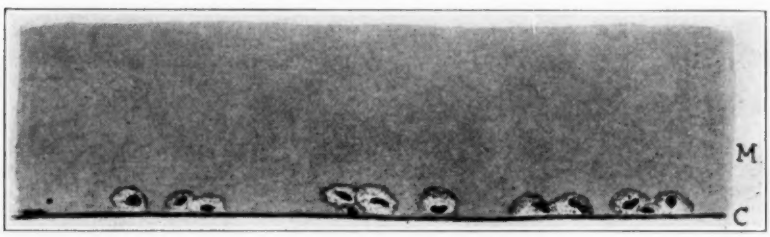

Fig. 7.—Phagocyte-like formations on the inner surface of the posterior capsule of the lens in a case of retinoblastoma in a globe of a boy 5 years of age. The tumor extends into the sheath of the optic nerve. The cataract is a morgagnian one. The drawing includes the posterior cortex of the lens with its capsule (*C*). The lens matter (*M*) is fluid. Lying in it, resting on the capsule, are groups of mononuclear, clear cells, containing double refracting particles, manifestly phagocytes. It would seem that in extraordinary circumstances cells on the external surface can make their way through the capsule. The fluidity of the lens indicates that there is no aperture in the capsule.

longer duration there were 2 instances of folds in the capsule worthy of mention. In the first case the globe was almost filled with a partly necrotic and perforating tumor that pressed the lens against the cornea.

In association with the general necrosis of the retina and uvea, the lens capsule was dissolved at one equator, and owing to its elasticity it had withdrawn into many folds. In the second case a tumor of the ciliary body had grown against the lens, causing such distortion and decrease in its volume that for want of support the stretch of the capsule adjoining the tumor fell into folds (fig. 8).

In explanation of the infrequency of folds in the capsule in the cases of tumor, it is enough to recall that a majority of the globes were glaucomatous and that with hypertony of the globe a lens has a tendency to swell and inflate the capsule, whereas with hypotony it has a tendency to shrink and let the capsule collapse.

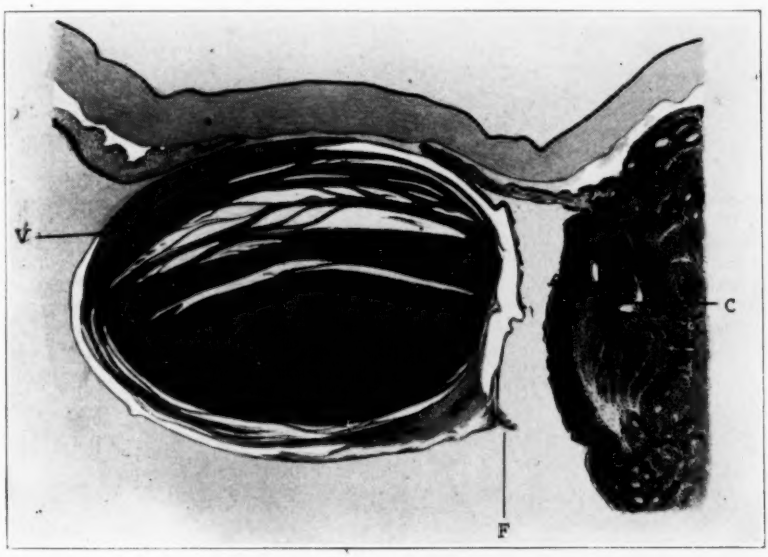

Fig. 8.—Vesicular cells on the side of the lens opposite that of absorption. A large malignant melanoma replaces the ciliary body and produces a wide area of iridodialysis. The collapse of the cornea is due to the fixation. A remnant of the ciliary body (*C*) rests on the projecting tumor. Fragments of the pigment epithelium adhering to the capsule indicate that the tumor touched the lens at the equator and caused the cortical layers to disappear under the influence of pressure. The capsule had become too large for its reduced content and therefore fell into elongated folds (*F*) at the point where the two bodies ceased to touch. On the opposite side of the equator a large number of vesicular cells (*V*) are grouped together. Here the iris shows little change.

2. *Proliferation of the Subcapsular Epithelium.*—The outstanding change in the subcapsular epithelium in the aforementioned papers on ulcers and scars of the cornea, spontaneous iritis and detachment of the retina was one of proliferating, exuberant character, often in the form of a large anterior polar cataract. However, in the cases of tumor of the present series, whenever there was any proliferation it was

as a rule restricted to a single layer of cells extending backward along the capsule. It must be due to the antagonism between distention of the capsule and proliferation of the underlying cells that anterior polar cataract is so seldom seen clinically in a glaucomatous globe. One of the few cases of anterior polar cataract was outstanding on account of the history, the anatomic changes and the uncertainty of the cause. The cataract occurred in a case of non-necrotic melanoma of the choroid that was thought to have existed for a long time because two years before enucleation a diagnosis of detachment of the retina was made. Transillumination revealed no tumor, and the age of the patient (17 years) was misleading. The globe increased in size, and an intercalary

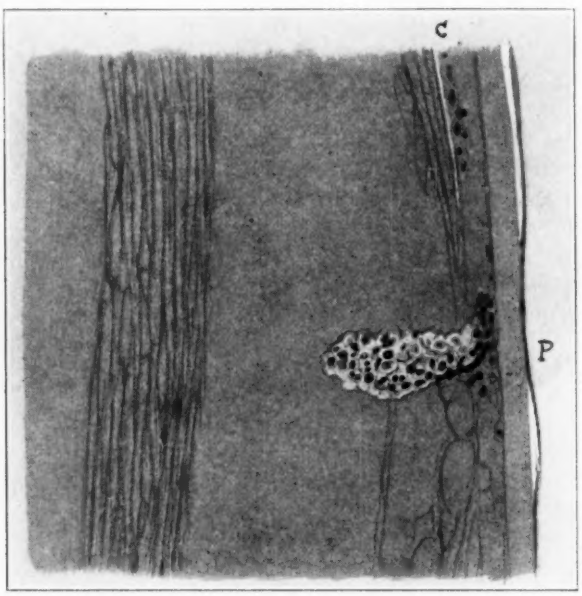

Fig. 9.—Desquamation and proliferation of lenticular epithelium in a case of a large necrotic malignant melanoma in a globe of a man aged 76 years. The iris, ciliary body and retina (not shown) are necrotic, as well as the cornea, which shows a ring abscess. In the fluid cortex anteriorly there is a row of desquamated cells (*C*) at one place; a sort of precipitate (*P*), composed of faintly staining hydropic mononuclear cells, extends into the depths of the liquefied lens.

staphyloma developed. Microscopic examination showed that the cataract extended under the iris far beyond the enlarged pupil. The retina was pressed against the staphyloma and the lens against the cornea. Blood vessels traversed the deep layers of the cornea. It is well known that the cornea, to the extent that a lens lies against it, becomes opaque but it is not absorbed. Had the cataract been confined to the pupillary area, it might have been argued that it represented a

reaction of the cells to pressure against the hard and resistant cornea; but as so much of it was protected under the soft iris pressure was excluded as a factor. Surely, the non-necrotic tumor could have played

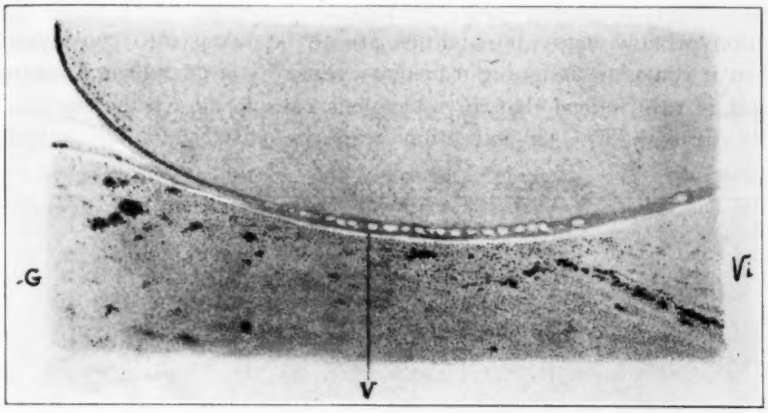

Fig. 10.—Subcapsular liquefaction in a case of retinoblastoma in a globe of a 4 year old child. Back of the equator a small, partially necrotic tumor touches the lens, which apparently has remained transparent. At the place of contact there is a row of oval vacuoles (*V*) lying on the inner surface of the capsule. They had undoubtedly formed in life, because they are located adjacent to the tumor and distant from it to the right there is only one vacuole. The vitreous (*Vi*) is filled with debris of the tumor, in which a few groups of nuclei represent surviving cells. To the left a wrinkled zonular fiber hangs to the lens capsule.

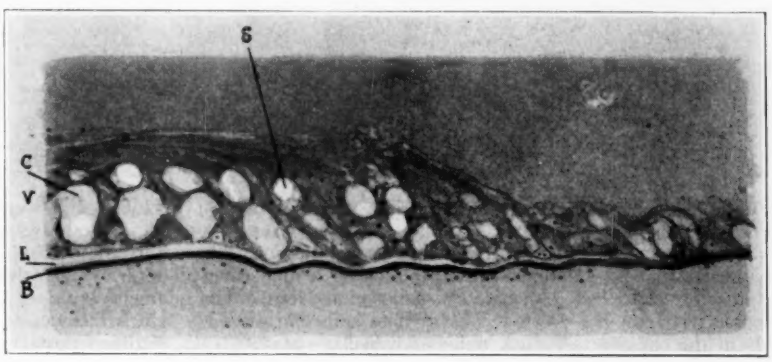

Fig. 11.—Vesicular cells containing vacuoles. A retinoblastoma invaded the papilla and choroid and caused the iris to shrink and the globe to enlarge. A greater part of the lens substance is cataractous. Posteriorly it is fluid. Anteriorly (not shown) there is a small subcapsular cataract. A partially necrotic tumor touches the lens back of the germinal zone, which is in order. Still farther posteriorly a great number of large, oval vesicular cells (*V*) lie along the inner surface of the capsule. It is unusual that within the walls of vesicular cells there should be empty spaces (*S*) in the midst of a faintly staining fluid (*C*). The narrow, densely staining band (*B*) along the posterior capsule of the lens (*L*) represents fibers of the compressed vitreous. In the fluid back of it a few separated cells float about.

no direct role, inasmuch as it was far separated from the lens by the detached and distended retina. It may have been that toxins from the subretinal fluid irritated the cells and caused them to proliferate. The globe being glaucomatous, increased tension could have had some effect in predisposing the lens to changes. Here is an illustration of how many possibilities are to be taken into consideration when it comes to assigning a primary cause for a complicated cataract.

It is rare indeed that an intact lens capsule allows the passage of cells through it. An exception was the case of a far advanced

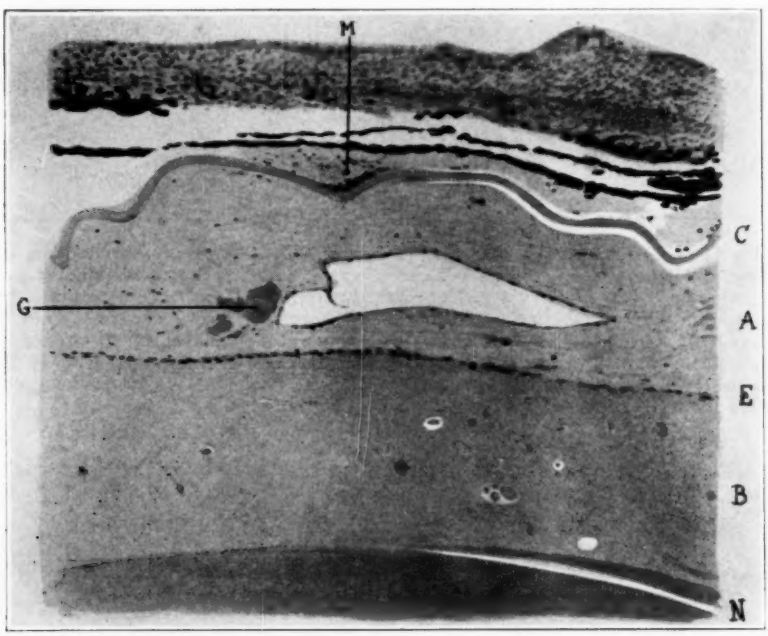

Fig. 12.—Cyst within the anterior capsular cataract in a globe of a woman aged 63. The eye had been blind for twenty years. Pathologic study reveals a partially necrotic malignant melanoma containing large fibrous membranes, as evidence that the tumor had been present for a long time. The drawing includes an anterior sector of a completely cataractous lens. The pigment layer of the atrophic iris is bound down in one area to a membrane (*M*) which fills out some folds in the capsule. A thick anterior capsular cataract (*A*), outlined posteriorly by a continuation of the capsular epithelium, detaches the wavy capsule from the lens substance proper. The cataract contains an empty cystic space, which is outlined by flat cells. To the left, globules of lens matter (*G*) are completely enclosed in the cataract. The anterior part of the cortex is fluid, but the nucleus (*N*) is homogeneous and seemingly solid. In the liquid cortex some bodies (*B*) float about, retracted from the fluid in the process of fixation.

retinoblastoma in a globe of a 5 year old boy. The lens capsule was apparently intact, distended and free of folds, and the subcapsular cells were but little disturbed. The germinal zone was gone. The sub-

stance was liquefied. Scattered in small groups along the internal surface of the posterior capsule was a row of cells that bore no resemblance to epithelial cells of the lens and, therefore, may have been phagocytes that had come through the capsule (fig. 7).

In spite of the fact that proliferation of the capsular epithelium was not a characteristic of the cases of intraocular tumors, there were instances in which the restricted proliferation showed unusual features.

(*a*) Druse of the Capsule: The lens in the case of the melanoma of the globe of the 17 year old girl previously mentioned showed a large druse applied to the capsule in the pupillary area. Its free surface

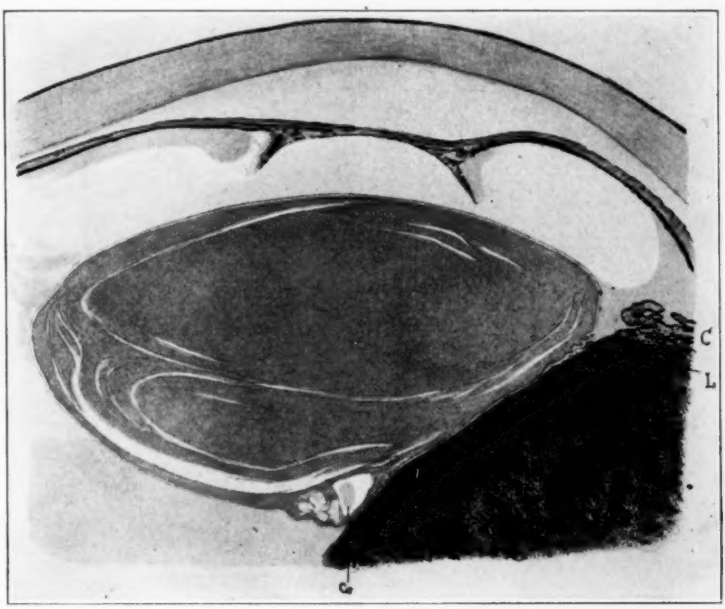

Fig. 13.—Cystic spaces caused by traction. A malignant melanoma of the choroid in the region of the ora serrata displaces the ciliary body forward (*C*) and compresses the lens. The pupil is not visible, but nearby pigmented tags from the iris approach the lens. A sector of lens matter has been absorbed along the area in contact with the tumor. The lens capsule is pressed forward at the equator (*L*), resulting in some ruffles. At the posterior angle of contact large cavities in the substance of the lens (*Ca*) are caused by traction on the capsule, which is adherent to the growing tumor. They contain a liquefied material. Nowhere else does the lens show signs of cataract.

was lined by a row of cells that had laid it down (fig. 1). Only once has such a formation been encountered before.

(*b*) Precipitate-Like Proliferation: Necrosis of the cornea with ring abscess and necrosis of the iris were the result of a large necrotic melanoma of a globe in a man aged 76. There was total liquefaction of the cortical substance. Some of the capsular cells had desquamated.

At one point they had proliferated and arranged themselves in a cluster hanging from the capsule into the liquid cortex like a bunch of grapes (fig. 9).

(*c*) Incipient anterior polar cataract: A melanoma in a globe of a man aged 72 caused total detachment of the retina, which, in turn, pressed the lens and the iris forward. The lens appeared to be normal except for two foci of cells that lay against the subcapsular epithelium in the pupillary area (fig. 15). The nuclei were compactly disposed, like those in a giant cell, and their cytoplasm had no borders. These

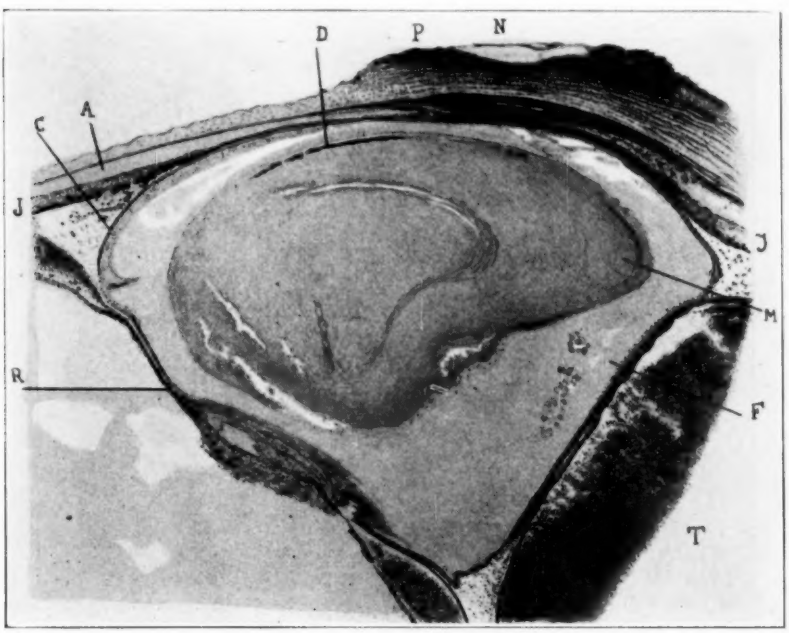

Fig. 14.—Morgagnian cataract and calcification in a case of retinoblastoma which involves the entire choroid (*T*) and extends into the optic nerve. The detached and degenerated retina and the tumor bulge forward to such a degree as to distort the lens into a triangular shape. The globe is buphthalmic, and an ulcer has destroyed the cornea. At *P* is the progressive border of the ulcer, with necrotic tags (*N*). The anterior chamber is slitlike (*A*). The iris (*I*) on both sides is atrophic and fixed to the lens. Behind the necrotic tag (*N*) the cornea shows a posterior abscess and pus lies in the anterior chamber. Of the capsular epithelium (*C*) only traces at the equator are to be seen. The lens is entirely cataractous. In the cortical mass of fluid (*F*) the nucleus is recognizable and forms a morgagnian cataract (*M*). On the nucleus the thinnest slivers of chalk deposit are noted (*D*), as symptoms of a long-lasting degenerative process in the lens.

cells were smaller than the overlying capsular cells. They could not have been lymphocytes, as there was no inflammatory reaction in the neighborhood and the aqueous was free of cells. The only explanation

was that they were derived from the subcapsular epithelium and were, in fact, the earliest beginning of an anterior polar cataract.

(*d*) Cystic Degeneration of Cortex: In a case of melanoma the entire cortical substance underwent a peculiar type of cystic degeneration (fig. 16). A fringe of lacelike cystic spaces enclosed the large, intact nucleus, the ruffled lens capsule forming the free border. Not a cell was seen in the lens; so the lens was apparently truly dead at the time of enucleation. Perhaps the fixation fluids had an immediate scalding effect, blistering the cortical layers of the lens.

3. *Necrosis of the Subcapsular Epithelium.*—In the preparations of malignant melanomas, necrosis of the epithelium of the lens went hand in hand with necrosis of the tumor. This was true even when

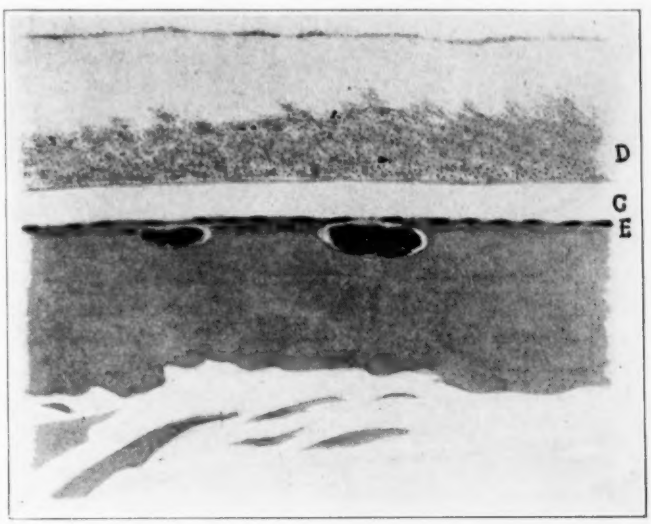

Fig. 15.—Early stage of anterior polar cataract in a globe of a man aged 72 years. A malignant melanoma of the choroid caused total detachment of the retina. The subcapsular epithelium has proliferated to form two small foci of cells (*E*). They resemble giant cells, as they contain many nuclei in a homogeneous protoplasm. It is not possible to differentiate the individual cells. The foci of cells apparently lie in cavities in the lens substance, as is suggested by the sharp border that stands out against the clear narrow zone surrounding each mass of cells. Between the two foci a few shadows of nuclei under the capsule are distinguished, owing to the oblique manner of sectioning. Lying on the capsule is cellular debris that originated in a deposit of albuminous fluid.

the necrosis of the tumor was partial. In cases of panophthalmitis produced by a totally necrotic melanoma dissolution of the lens capsule, death of the epithelium and destruction of the substance are but a part of the general necrosis of the retina, uveal tract, cornea and sclera.

A comparison of the state of the cells in the pupillary area with that of the germinal cells at the equator in the cases of malignant

melanoma revealed that not infrequently the anterior cells were preserved when the equatorial cells were gone. Altogether, the impression grew that the anterior capsular cells are more resistant to insult than the equatorial, germinal, cells. The necrotic melanomas seemed to possess greater toxicity than necrotic retinoblastomas; in other words, the uveal tumors were more destructive to the lens than the retinal tumors. Consequently, death of the lenticular epithelium to any great extent was a rarity in the cases of retinoblastoma.

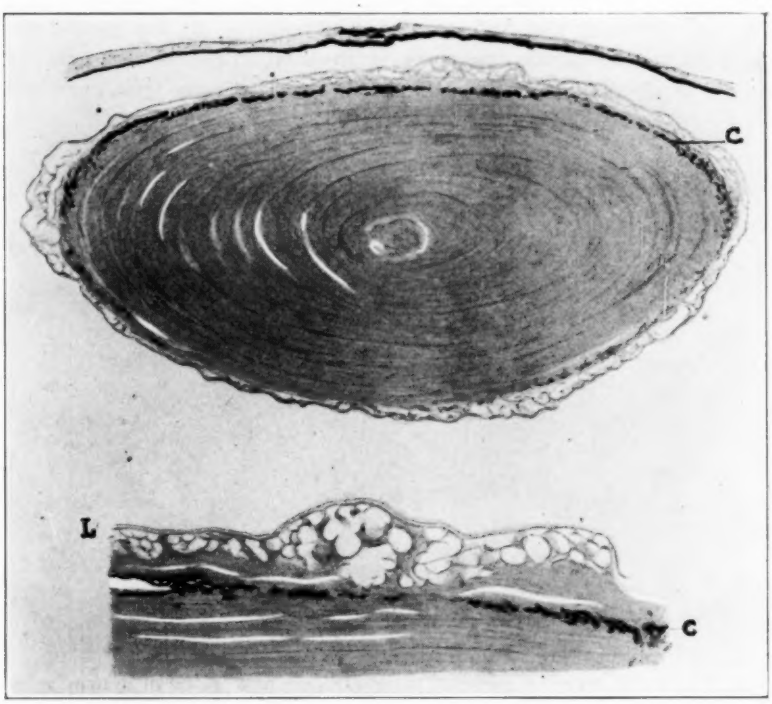

Fig. 16.—Lacelike cystic degeneration of the cortex and calcification of the lens in a case of malignant melanoma of the choroid. The iris is necrotic. The capsule is very wavy, but the bulk of the lens substance appears to be solid. A file of chalk granules (*C*) caps the nucleus anteriorly. A narrow zone immediately under the entire capsule is occupied by vacuoles of different sizes. The spaces are empty, but they do not seem to be artefacts.

The detail of the lens (*L*) from the anterior surface shows no capsular epithelium. The calcification is made up of relatively small granules that form a continuous row. In place of the usual homogeneous liquefaction of the cortex there is a delicate, lacelike fringe.

There were 2 glaucomatous globes in which the melanoma showed practically no necrosis but still the pupillary epithelium of the lens was gone, leaving the epithelium elsewhere unaffected. Such a condition in the pupillary area is usually caused by toxins coming directly from

the cornea. In each of these globes necrosis of the iris and the ciliary epithelium was present. It was believed that the necrosis in the three separate areas resulted from malnutrition caused by a high and sudden increase in the intraocular tension.

Illustrating universal necrosis within the globe associated with a necrotic tumor, there were 18 cases of necrosis of the iris, in 6 of which the necrosis was confined to the pupillary zone; 17 cases of necrosis of the ciliary body, in 6 of which only the processes were dissolved, and 17 cases of necrosis of the retina. It is known from other experience that, although necrosis of the ciliary body and iris occurs during an attack of acute fulminating glaucoma, the retina nearly always escapes damage. In the preceding 17 cases in which the retina was intact it was concluded that toxins from the tumor, and not glaucoma, were responsible for the disappearance of the lenticular cells.

An informative case of melanoma was one in which the death of the epithelium accurately corresponded in extent to a necrotic area of the iris that overlay it (fig. 3). The ciliary processes on the same side as the necrotic part of the iris were dissolved. The anterior chamber, containing cellular elements, was present. Three explanations as to the relation between the necrosis of the iris and that of the underlying cells of the lens come to mind: First, the iris and ciliary epithelium became necrotic simultaneously as a result of toxins from the tumor. It was true that slight necrosis was present in the tumor, but this was too insignificant to account for damage elsewhere. Second, the iris and the ciliary processes became necrotic as a result of secondary glaucoma, and then, afterward, as a result of toxins from the overlying necrotic zone of the iris, death of the subcapsular epithelium followed. Third, the necrosis of the epithelium was due to lack of nutrition from the ciliary body after the circulation had been impeded by secondary glaucoma.

As between the second and the third explanation, I prefer the second, because if really impaired nutrition had been the cause a loss of the epithelium in the pupillary area should have been found. Clinically, the globe was recorded as very hard and the iris as being of the dull gray characteristic of glaucoma. It would be well to study the effect of necrosis of the iris on the subcapsular epithelium in cases of glaucoma.

4. *Effect on the Lens of Direct Contact of the Tumor.*—In the play of a tumor against a lens, it is remarkable that the lens retains its transparency even when a large part of its substance has been removed (fig. 4). This fact was first observed long ago, but even today it surprises the pathologist, not so much because lens matter disappears as a result of pressure atrophy as because the remaining lens substance does not become opaque. Anatomically, according to the preparations,

pressure not only causes simple disappearance of the lens fibers but in doing so may displace and distort them and interfere with their normal development.

Strange to say, in 1 of the cases of melanoma of the ciliary body, vesicular cells, in addition to the few near the tumor, were seen in larger quantity on the opposite side of the equator, as far away from the tumor as possible (fig. 8). Only the lens capsule separated the hard nucleus from the tumor. Probably by way of the resistant nucleus, indirect pressure was exerted on the opposite germinal zone. A tumor, in so far as it covers the surface, must prevent the diffusion of the aqueous through the capsule and so interfere with the nutrition of the lens.

It is strange that a tumor in compressing a lens seldom produces dislocation. Apparently, a lens may more easily lose its colloid substance or become distorted than be uprooted from its attachments to the ciliary body and vitreous. This is all the more remarkable as the zonular fibers on the side of the tumor are relaxed, so that the lens can readily be shifted in the opposite direction.

5. *Changes in the Lenticular Substance.*—Frequently cataractous changes were noted in the anterior and posterior cortex, whereas the equator, the area of predilection for senile cataract, was less often affected. In 6 of the cases of melanoma and in 1 of the cases of retinoblastoma disintegration throughout the lens was noted; that is, the substance was broken up into pieces.

Of the total number of 57 cataracts, 24 showed liquefaction in varying amounts. Eleven of these 24 cataracts were associated with retinoblastoma and 13 with malignant melanoma. In practically all the cases of melanoma the liquefaction was partial, because this is a tumor of older people, in whom the nucleus of the lens cannot be dissolved. The term "liquefaction of the lens" when applied to the young conveys the idea of fluidity throughout; when used for persons of maturer years it is understood that only the cortex is fluid. The transformation of solid lens matter into liquid form seemed to be a characteristic effect of the toxins produced in the decay of a malignant melanoma.

It was striking that in 4 of the cases of necrotic retinoblastoma, the youngest patient being a child of 1 year, faint outlines of what is known as the "embryonic nucleus" could be traced (fig. 5). From this observation it was deduced first, that at this early age the embryonic nucleus as it is recognized with the slit lamp not only is an optical phenomenon but is in reality a differentiated center. This is demonstrated again in zonular cataracts, in which a distinct central opacity accurately corresponds to the embryonic nucleus. It may happen that after the

needling of a congenital cataract the nucleus appears in toto in the anterior chamber.

Second, it was made clear, at least in the 4 cases, that the embryonic nucleus is more resistant than the cortex to toxins in the fluids of metabolism; otherwise it would have been liquefied.

6. *Calcification of Lens Substance.*—A deposition of calcium was seen in the lens in 3 of the cases of retinoblastoma. This was an impressive finding, because an intraocular tumor is rarely of such long duration as to afford time for calcification. In the first case there was a deposit of chalk along the surface of the nucleus in connection with an anterior polar cataract which was thought to have been caused by iritis that antedated the retinoblastoma. In the second case the globe was buphthalmic, and the tumor had extended to the outside, indicating a condition of long standing. In this case a crust of chalk accurately surrounded the surface of the nucleus (fig. 14). In the third case, in which the condition was also of long standing, the cataract was not a typical morgagnian one, because the cortex was not fluid but had broken up into debris. Here the chalk, also caplike, was deposited around the nucleus of the lens (fig. 2). These 3 cases afford further proof that as early as the first year of life the nucleus exists as a true physiologic unit.

There was a single instance of membranous cataract. This occurred in the case of the epithelial tumor of the ciliary body which led to a dense membrane with bone in the circumlental space.

7. *Cystic Space.*—A comparatively large cavity, the first of its kind observed in this series, was encountered in a case of glaucoma with a small retinoblastoma (fig. 1). The lens in general deviated little from the normal. At the posterior pole a cystic space caused the capsule to bulge backward. The space was not lined with epithelium, and although it contained an albuminous fluid it was set down as an artefact. In another case, that of a mushroom-shaped melanoma, the tumor flattened the equator of the lens and, by dragging on the capsule, produced a dislocation of the fibers and with it two cavernous spaces (fig. 13). In a case of necrotic melanoma in which the patient had been blind for twenty years, a flat cystic space developed, as a curiosity, near the center of an anterior polar cataract (fig. 12). Finally, as a result of contact with a necrotic retinoblastoma, a row of vacuoles developed along the internal surface of the posterior capsule, giving rise to an interesting detail not described before (fig. 10).

8. *Vesicular Cells.*—Of the 57 cases of cataract, the lens contained vesicular cells in only 13 of the cases of melanoma and 5 of the cases of retinoblastoma, and then usually in small amounts. These cells were nearly always located in their characteristic places at the equator and

posteriorly (fig. 11). Vesicular cells speak for an arrest in development of lens fibers, the causes being not so great as to destroy the cells outright.

9. *Localization of the Lens.*—Particular attention was paid to the location of the lens, because misplacement of itself may cause cataract. In 14 cases the lens was pressed forward by a tumor that filled out the entire globe, the growth being a retinoblastoma in 2 cases and a melanoma in 12 cases. There were 11 cases of forward dislocation in which the tumor was too small to fill out even half the globe. Here the pressure was exerted by fluid accumulating under a detached retina. In 7 cases, 2 of retinoblastoma and 5 of malignant melanoma, the lens had fallen back, owing to liquefaction of the vitreous and destruction of the ciliary epithelium to which the zonular fibers were fixed. In a number of cases there was a slight dislocation to one side.

10. *Tension.*—The results of clinical examination were not always available, but histologically there was enough evidence for one to judge that most of the globes had been hard, or very hard, at the time of enucleation, or at least had been glaucomatous at some period. The question arose as to what effect, in general, the increased tension had on the production of the cataracts. Taking into consideration the advanced changes in the lenses and the relatively short duration of the glaucoma, it was decided that in most cases the diminished metabolism resulting from the glaucoma did little more than predispose the lens to cataract.

CLINICAL ASPECTS

In a case of ordinary cataract, considering the opaqueness of the lens, it is surprising how bright the pupil stands out by transillumination. Should there be an absence of red light through the pupil when the beam of the lamp is placed at a certain place at the equator, it is probable that a melanoma of the choroid is present, provided the patient is an adult. However, the lesion is by no means always a tumor, since an old subretinal hemorrhage may be transformed into a large amount of pigment and thus throw a shadow. On the other hand, a leukosarcoma throws no shadow. In every instance in which there is a combination of cataract and glaucoma, and there is the slightest possibility of the presence of an intraocular tumor, it is advisable to recommend the removal of the globe.

In a case of cataract in an infant's globe the age gives a diagnostic hint, the occurrence of retinoblastoma after the age of 4 years being exceptional. In childhood metastatic ophthalmia, conglomerate tuberculosis of the choroid and, in rare cases, Hippel's disease (angiogliomatosis of the retina) may produce cataract and secondary glaucoma.

Tuberculosis progresses rapidly and is not very toxic, so that usually there is not time for the development of a total cataract.

The differentiation between retinoblastoma and metastatic ophthalmia is most important. If the lens is still sufficiently transparent, areas of normal retina with here and there chalky white spots look quite different from a grayish, slimy exudate behind the lens or from a smooth, organized membrane. Retinoblastoma stands out more distinctly than an exudate because the vitreous is clearer. At the same time, through the wide pupil, tremulous particles from the tumor may be visible in the circumlental space. No matter whether the lens is entirely opaque or not, the indication for enucleation of an infant's globe is not urgent so long as consensual reaction of the pupil is present. At first a retinoblastoma confines itself to replacing the retina, and therefore reliance can be put on the certain sign that as long as consensual reaction is present not all of the retina is replaced and the optic nerve is not yet involved. In every case of an infant's globe in which the pupil is wide, the lens is cataractous and glaucoma is present, particularly if the globe is enlarged or becomes so while under observation, enucleation is indicated.

SYPHILITIC UVEITIS

Diagnosis, Herxheimer Reaction and Results of Various Treatments, Including Penicillin Therapy

JOSEPH V. KLAUDER, M.D.
AND
GEORGE J. DUBLIN, M.D.
PHILADELPHIA

SYPHILIS AS ETIOLOGIC AGENT

SYPHILITIC uveitis [1] characteristically occurs in the secondary or late secondary stage of syphilis. When there is clinical evidence of early syphilis, a positive Wassermann reaction and prompt retrogression of the ocular inflammation after antisyphilitic treatment, the diagnosis offers no difficulty.

How valid is the diagnosis of syphilitic uveitis based solely on a positive Wassermann reaction? Or how sound is such a diagnosis in the late stage of syphilis or when the duration of the infection is unknown? What are the criteria of efficacy of antisyphilitic treatment

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From the Clinic for Treatment of Ocular Syphilis, Wills Hospital.

Read at a meeting of the College of Physicians, Philadelphia, Section on Ophthalmology, Dec. 21, 1944.

An abstract of this paper, with discussion, was published in the May 1945 issue of the ARCHIVES, page 416.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Wills Hospital.

The results which have been presented in this paper must be interpreted in the light of the fact that from June 1943, the date of inception of the study, to the present time commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency, in terms of units per milligram, has increased. The relative amounts of the several identified penicillin fractions, G, F, X and K, have likewise varied from time to time. These two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

1. The term "uveitis" used throughout this paper includes inflammatory processes of the anterior uveal tract clinically diagnosed as iritis, cyclitis and iridocyclitis with or without secondary involvement of the cornea. The term is used with the implication that an inflammatory process of the anterior uveal tract is not confined to one component part. Inflammation of the anterior uveal tract of congenital syphilis is not included in this study.

to justify the conclusion that uveitis was caused by syphilis? Antisyphilitic treatment exerts a nonspecific effect on uveitis.

Judgment at times is difficult, since local treatment and nonsyphilitic therapy also exert a favorable action on uveitis. The purpose of this paper is to discuss these considerations, as well as the Herxheimer reaction [2] of the ocular lesion as evidence of syphilitic causation. The intensification of the inflammatory process (constituting the Herxheimer reaction) was evaluated with the corneal microscope and the slit lamp before and after antisyphilitic treatment. The Herxheimer reaction as observed with the biomicroscope has not been studied as a diagnostic aid.

There are no distinctive features of serous or plastic iritis to warrant the diagnosis of syphilitic causation. The nodular type is more characteristic; confusion, however, may arise with nodular iritis due to other causes, namely, tuberculosis, sympathetic ophthalmitis, sarcoidosis, severe leukemia, caterpillar hairs, leprosy and neoplasm.

Igersheimer [3] stated the opinion that iritis appearing after the third year of infection should not be regarded as syphilitic unless there is a favorable response to antisyphilitic treatment. He expressed the belief that syphilis is rarely the cause of iritis in the late stage of infection. We subscribe to this opinion.[4]

It is our impression that the criteria of syphilitic uveitis used by most writers reporting on its incidence were positive serologic reactions and response to antisyphilitic treatment. Few authors have defined their criteria of diagnosis. Authors reporting on a large series of patients with syphilitic uveitis or iritis (Groenouw,[5] Talbot,[6] Zimmermann,[7] Moore [8]) have included patients in the late stage of syphilis. In the

2. This well known reaction of inflamed syphilitic tissue, first described by Jarisch and later by Herxheimer, is more properly called the Jarisch-Herxheimer reaction.

3. Igersheimer, J.: Syphilis und Auge, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 17, pt. 2, pp. 205-227.

4. Dr. Marjory K. Hardy reviewed the case records of patients who had active lesions of syphilis in various stages of the infection to determine the percentage who had inflammation of the anterior uveal tract. The result of this review follows. Primary syphilis: Of 79 patients (all males) who had a chancre observed in the presecondary stage of syphilis, none had iritis. Secondary and late secondary syphilis: Of 111 patients, 40 per cent of whom were Negroes, 4 had iritis (3.6 per cent). Late syphilis: Of 86 patients with lesions of late syphilis affecting the skin, mouth, throat or bone, none had iritis.

5. Groenouw, A., in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, Leipzig, W. Engelmann, 1904, vol. 11, pp. 737-862,

6. Talbot, A.: Recherches statistiques sur la syphilis de l'œil, Thesis, Bordeaux, no. 18, 1894.

7. Zimmermann, E. L.: Syphilitic Iridocyclitis with a Consideration of Factors Influencing Its Occurrence, Arch. Ophth. **53**:549-565, 1924.

8. Moore, J. E.: Syphilitic Irtis, Am. J. Ophth. **14**:110-126, 1931.

series reported by Moore [8] and by O'Leary [9] patients were included who gave no response to antisyphilitic treatment. It is doubtless this reason, and other considerations, that prompted Moore to state in his paper that confusion may arise in his group of patients with late syphilis concerning the role of this disease versus other etiologic factors.

In the study by Guyton and Woods [10] of the causes of uveitis in 562 cases the etiologic role, either definite or presumptive, was attributed to syphilis in 59 cases, or 10.5 per cent of the entire series. Of these, syphilitic uveitis was present in 36 cases, choroiditis in 7 cases and generalized uveitis in 16 cases. Congenital syphilis was present in 22 cases and acquired syphilis in 37 cases.

These authors stated the opinion that with the history, results of physical examination, serologic reactions and response to antisyphilitic therapy pointing to syphilis as the cause of uveitis a positive diagnosis presented little difficulty. For this reason, the diagnosis for the greater number of syphilitic patients in their group 1 could be classified as clearcut.

Their criterion for a definite diagnosis of syphilitic uveitis were as follows: (1) a characteristic uveal lesion, with nodules or gummas, occurring in the course of either early or late syphilis but in the proper time relation to the acquisition of the syphilis; (2) a lesion which was noncharacteristic of syphilis but which occurred at the proper stage of early syphilis and responded favorably to antisyphilitic treatment, or (3) a uveal lesion which appeared as noncharacteristic but which occurred in the late stage of syphilis and responded favorably to proper antisyphilitic treatment in a patient with no other demonstrable etiologic factor.

The patients in our series, in addition to syphilis, frequently had other pathologic processes which are regarded as causing uveitis. The significance of a favorable response to antisyphilitic treatment was somewhat invalidated, since we observed that such treatment exerted a nonspecific effect (case 5).

Woods [11] reviewed published statistics on the etiology of uveitis. It is of interest to note that earlier authors attributed to syphilis an incidence as high as 70 per cent in cases of uveitis. More recent statistics, on the other hand, have shown a steady decrease in the incidence of syphilis (now given as from 10 to 17 per cent) and of "rheumatism," whereas the incidence of foci of pyogenic infection and of tuberculosis

9. O'Leary, P. A.: Syphilis in Etiology of Uveitis, Am. J. Ophth. **15**:24-26, 1932.

10. Guyton, K., and Woods, A. C.: Etiology of Uveitis, Arch. Ophth. **26**: 983-1013 (Dec.) 1941.

11. Woods, A. C.: Syphilis of the Eye, Am. J. Syph., Gonor. & Ven. Dis. **27**:133-186, 1943.

has increased with the inclusion of new causes (sarcoidosis and brucellosis).

In Woods's [11] study of syphilis of the eye, it is stated that iritis is by far the most important of the ocular lesions of early syphilis, that it accounts for 73.3 per cent of the total ocular complications of early syphilis and occurs in about 4 per cent of all cases of early syphilis and that in general from 30 to 40 per cent of all cases of iritis are attributable to syphilis.

HERXHEIMER REACTION (THERAPEUTIC SCHOCK)

The Herxheimer reaction is the aggravation of a syphilitic lesion following the initial administration of a spirocheticidal medicament. The more acute the syphilitic inflammation, the more active the spirocheticidal medicament, the larger the dose or the more direct the method of administration that exerts greater spirocheticidal action (intravenous versus intramuscular injection), the more pronounced is the Herxheimer flare. The reaction is best seen during the secondary eruption of syphilis after intravenous injection of a large dose of an arsenical.[12]

Herxheimer Reaction After Arsenical Therapy.—Soon after the advent of arsphenamine the occurrence of the Herxheimer reaction was reported with a variety of ocular lesions caused by syphilis (Flemming,[13] Gallemaerts and Kleefeld [14]). Toulant [15] suggested the Herxheimer reaction as a means of diagnosing syphilitic lesions of the eye. In Zimmermann's [16] studies of ocular syphilis the Herxheimer reaction is

12. The reaction as originally described was a local one, an accentuation of the secondary eruption of syphilis occurring within twenty-four hours after the use of a mercurial. Its occurrence after the advent of neoarsphenamine was given as proof of the spirocheticidal action of the drug. (This applies now to the reaction occurring after the initial injection of penicillin.) Before the discovery of Treponema pallidum the Herxheimer reaction was used for diagnostic purposes. The reaction is attributed to endotoxins arising from massive destruction of the spirochetes. In addition to this "local" reaction, a "general" reaction was described, characterized by transitory increase in the headache of neurosyphilis and in the lightning pains of tabes. At the present time the term "Herxheimer reaction" is used in a still more general way than the "general" reaction. It was given as the explanation of the reaction in the "provocative" Wassermann test. It is used to explain local reactions other than in the original sense, for instance, a rupture of an aneurysm following administration of arsphenamine or acute yellow atrophy of the liver subsequent to jaundice and arsenical therapy.

13. Flemming: Wirkung von Salvarsan auf das Auge, Arch. f. Augenh. **78:** 197-211, 1911.

14. Gallemaerts, E., and Kleefeld, G.: Etude microscopique de l'oeil vivant, Ann. d'ocul. **157:**152, 1920.

15. Toulant, P.: Les reactions oculaires consecutives au traitement specifique des syphilis de l'oeil: Leur valeur diagnostique, Arch. d'opht. **40:**215-227, 1923.

16. Zimmermann, E. L.: The Role of the Arsphenamines in the Production of Ocular Lesions, Arch. Ophth. **57:** 509-530, 1928.

discussed. He recognized three expressions of the reaction involving the anterior uveal tract: (1) as uveitis in an eye previously free from all clinical changes, (2) as an exacerbation of an old quiescent iritis and (3) as an intensification in an already acute iritis.

To our knowledge, the Herxheimer reaction has not been studied in a series of patients with inflammation of the anterior uveal tract in order to determine whether the reaction, as observed with the biomicroscope, could serve as a means of differentiating a syphilitic and a nonsyphilitic process.

In our study of the diagnostic value of the Herxheimer reaction the following patients were employed: patients whose iritis or uveitis was associated with lesions of early syphilis (these patients comprised group 1, discussed later) and a group of 36 patients consecutively seen with inflammation of the anterior uveal tract who did not have clinical evidence of syphilis. For some the Wassermann reaction was negative, for others positive. The uveitis in some was regarded as nonsyphilitic and was associated with other pathologic processes causing uveitis, such as sarcoidosis. The group also included patients with late syphilis who had had considerable antisyphilitic treatment. Such patients were included to serve as controls.

These patients were examined with the corneal microscope and the slit lamp a short time before and sixteen to twenty hours after an intravenous injection of 0.45 to 0.6 Gm. of neoarsphenamine. A comparison was made of the degrees of inflammation observed in the two examinations. The observations were correlated with the history, the clinical evidence and the result of antisyphilitic treatment. All patients with positive Wassermann reactions were given antisyphilitic treatment. The Herxheimer reaction[17] was regarded as positive if on second examination it was observed that the haziness of the cornea was increased, the aqueous was more turbid and contained an increased number of inflammatory cells, corneal precipitates were increased and the iris was more swollen (cases 1, 2 and 3). Usually the intensification of the inflammatory process was decisive, leaving no doubt as to a positive reaction. In some cases the intensification was less pronounced, and in a few cases evidence of intensification was essentially an increased number of inflammatory cells and/or a greater number of corneal precipitates. One patient who had iritis associated with lesions of early syphilis was examined eight hours after the injection of an arsenical.

17. Microscopic evaluation of the Herxheimer reaction is unique. As aforementioned, the reaction is apparent macroscopically or by an increase of subjective symptoms. Although we are unacquainted with any published studies of a microscopic or histologic phase of the reaction, it necessarily follows that there is such a phase. An indurated or scarred remains of a chancre would doubtless show a histologic reaction that would not extend to gross evaluation.

At this time the Herxheimer reaction was positive. In another patient (case 1) the Herxheimer flare was abating on reexamination twenty-seven hours after is was observed. Apparently, a positive reaction can be observed from eight to about twenty-four hours after the initial injection of an arsenical. We did not determine the minimum dose of neoarsphenamine that will produce a Herxheimer reaction or the earliest period in which it is observed.

Herxheimer Reaction After Penicillin Therapy.—The Herxheimer flare was not uniformly observed in the 17 patients in this series whose iritis associated with lesions of early syphilis was treated exclusively with penicillin. The absence of the reaction may be explained in some patients with severe iritis by reason of the purposely reduced doses of penicillin employed at the onset of treatment in order to modify the *force majeur* of initial large doses. However, in 1 patient the reaction was observed as an accentuation of the cutaneous eruption and in another as increased swelling of the cervical lymph nodes without ocular reaction.

In 2 patients the reaction was pronounced after increasing doses of penicillin had reached 50,000 units. With 1 of these patients this dose was then halved and treatment continued in ascending doses from this level. In the other patient there was an increase of intraocular tension when the dose of penicillin approached 50,000 units, on the third day of treatment. Injections were stopped for twenty-four hours and resumed with smaller doses.

The Herxheimer reaction of iritis treated with penicillin is detailed in the report of case 3. The intensification of the inflammation was noted on examination with the slit lamp eighteen hours after an initial injection of 10,000 units of penicillin, followed by additional doses of 10,000 units every four hours until the time of examination with the slit lamp. An additional reaction was transitory pain in the affected eye three hours after the initial injection of penicillin

Herxheimer reactions as observed in treatment of syphilis in general are likely to be more pronounced after penicillin therapy than after other chemotherapy. This is evidence of the active spirocheticidal action of penicillin and necessitates reduced initial doses in the treatment of acute inflammatory lesions of ocular syphilis.

Status of the Herxheimer Reaction as a Diagnostic Aid.—Of our patients with uveitis associated with late secondary syphilis and of the patients with iridorecidivism (groups 1 and 2, later discussed) the reaction was observed in 70 per cent and was not observed in 30 per cent. Nine patients, or 25 per cent, of the 36 patients with uveitis unassociated with clinical evidence of syphilis had a positive Herxheimer reaction which was regarded as false, or not indicative of syphilitic causation. It is therefore concluded that the reaction cannot be regarded

as an absolute criterion in differential diagnosis of syphilitic inflammation of the anterior uveal tract.

Is the Herxheimer Reaction Harmful? The Therapeutic Paradox.—Many writers discuss the Herxheimer reaction of ocular lesions only in relation to the desirability of avoiding initial energetic antisyphilitic treatment in order to produce a more gradual subsidence of the acute phase. As aforementioned, the Herxheimer reaction is a focal flare-up of the lesion following initial injection of a spirocheticidal agent. In mild or moderately inflamed lesions of the anterior uveal tract this focal flare is not productive of harm. What is potentially harmful is the end result of continued energetic antisyphilitic treatment, which produces too rapid retrogression and causes additional damage by fibrosis in too rapid healing—this is called the therapeutic paradox.

In initiating treatment of syphilitic uveitis or iritis, we were guided by the degree of inflammation and the presence of complications. For patients with a mild to moderate degree of inflammatory reaction and without complications (the majority in this series were of this type) routine antisyphilitic treatment was employed. In these patients an initial injection of 0.45 Gm. of neoarsphenamine did not result in unfavorable end results whether or not the Herxheimer reaction occurred. Initial treatment was modified in cases of the following processes—severe plastic iritis associated with considerable or complete pupillary occlusion; hypopyon or plastic exudate in the pupillary area; broad synechias; increased intraocular pressure and the nodular type of iritis, which always tends to destruction of tissue and its replacement with connective tissue. In such cases it is necessary, in order to avoid the therapeutic paradox, that early treatment be of a mild character. Fever therapy may first be employed (consisting of three to four inductions of fever) or one or two injections of a soluble bismuth compound prior to initial injection of 0.1 or 0.2 Gm. of neoarsphenamine. Subsequently this amount is increased to a full dose.

SYPHILITIC UVEITIS: REPORT OF SEVENTY-TWO CASES

Of the 72 patients, 42 were males and 30 females; 50 were Negroes, of whom 28 were males. Of the 22 white patients, 14 were males. The age range was from 21 to 63 years. Of the 72 patients, 55 had unilateral and 17 bilateral uveitis. Fifteen patients had the nodular type of iritis[18] (iritis papulosa, iritis nodulosa, gumma of the iris);

18. The node or papule of the nodular type of iritis is regarded as comparable to the papule of the secondary eruption of syphilis. Igersheimer [3] stated the opinion that the longer syphilitic iritis persists, the greater the likelihood of nodular (papular) formation. The statement applies to a macular eruption of syphilis. The longer it persists the greater the likelihood of papules. In the cutaneous

the nodules were always confined to one eye, no instance of bilateral nodular iritis being seen. Nodular iritis was more frequently observed in cases of iridorecidivism, being present in 7 of 12 cases, in contrast to 9 of 58 cases of iritis not of the iridorecidivous type. Nodules not apparent on gross examination were observed through the corneal microscope. The nodular type has been described by a number of authors (Groenouw,[5] Igersheimer,[3] Duke-Elder[19] and Woods[11]) and need not be discussed.

Of 78 cases of syphilitic iritis reported by Igersheimer,[3] the disease was bilateral in 25 and of the nodular type in 31.

Our 72 patients with uveitis were divided into three groups: (1) 53 patients with other lesions (diagnostic) of secondary or late secondary syphilis, (2) 12 patients with iridorecidivism and (3) 7 patients with no clinical (diagnostic) evidence of syphilis.

Group 1.—Ocular involvement was most frequently seen in the late stage of secondary syphilis,[20] at the time the eruption was disappearing or had almost retrogressed, or in a still later stage of mucocutaneous relapse.[21] The predominating type of eruption was the small follicular syphilid, occurring in patches or groups. Fifteen patients had this type, and an additional 17 presented a larger type of papular syphilid. The small follicular syphilid was conspicuous among the Negro patients, who also had pronounced polyadenitis and some arthritic symptoms involving one or more joints.

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evolution of syphilis following the secondary stage of syphilis the nodule, the gumma and the gummatous ulcerative lesion appear. If, in the evolution of syphilis, iritis is a part of the secondary or late secondary eruption, the next lesion, reasoning by analogy, is a destructive one, such as the gumma. According to this analogy, one would not expect iritis of syphilitic origin to appear much later than five years after infection. Beyond this period the occurrence of mucocutaneous lesions that belong in the category of secondary or late secondary syphilis is rare. This analogy applies to the skin. It does not apply to other systems, notably the nervous system. These considerations explain the greater frequency of nodular iritis in patients with iridorecidivism.

19. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1944, vol. 3.

20. Of the few patients seen before the chancre has disappeared, 1 presented a chancre on the arm. The lesion was excised and the material emulsified and injected into the testes of rabbits, in an attempt to isolate an ocular strain of T. pallidum. The purpose of this study was not achieved (Klauder, J. V.: Ocular Syphilis: Factors Influencing the Localization of Syphilis in the Eye, Arch. Ophth. **7**:268-279 [Feb.] 1932).

21. The studies of Brown and Pearce (Experimental Production of Clinical Types of Syphilis in the Rabbit, Arch. Dermat. & Syph. **3**:354 [March] 1921) furnished evidence that immunologic response of the rabbit to syphilitic infection is a factor in determining ocular localization in this animal.

Other writers have emphasized the frequency of a papular type of eruption associated with iritis. Zimmermann [7] and Moore,[8] especially, stressed the frequency of iritis in the Negro and its association with a folliculopapular syphilid, polyadenitis and syphilitic arthritis (usually of the ankles). These authors regard this association of symptoms as a clinical syndrome—a racial predisposition. Our study gives emphasis to the observation of these authors.

Group 2.—Iridorecidivism (iridorelapse) is the occurrence of iritis after insufficient treatment of early syphilis. In its biologic significance it corresponds to neurorecurrence (neurorecidivism). Soon after the advent of arsphenamine, it was thought that a few injections sufficed to effect a cure. It was observed that such inadequate treatment predisposed to an increased incidence of neurosyphilis. In explanation of both phenomena, it is believed that insufficient treatment of early syphilis predisposes the patient to recurrence by interference with the resistance-building mechanism.

In a series of 190 cases of syphilitic iridocyclitis reported by Zimmermann [7] there were 21 instances of iridorecidivism; and in a series of 140 cases of iritis of early syphilis reported by Moore [8] there were 29 such instances. In these series, iritis appeared after a lapse of treatment comprising for the majority of patients six or less injections of arsphenamine. The interval between the lapse of treatment and the appearance of iritis varied in most cases from four to sixteen weeks.

A notable feature of iridorecidivism is the likelihood of the absence of other clinical evidence of syphilis and a negative or partially positive Wassermann reaction. In 68 per cent of the cases in Moore's series there was no other clinical evidence of syphilis, and the Wassermann reaction was negative in 45 per cent. The history of recent lapse of treatment is an important consideration in diagnosis of iridorecidivism; this applies especially to the Negro, since syphilitic uveitis is more frequent among Negroes and they cooperate poorly in therapy of the systemic infection.

Of our 12 patients with iridorecidivism (cases 2 and 4), 8 were Negroes (4 males and 4 females), and the remaining 4 were white males. The previous treatment varied from five to ten injections of an arsenical or a bismuth compound, followed by a lapse of treatment ranging from four to ten weeks, except in 1 case, in which it was four months. In 2 patients iritis occurred in the second eye after lapse of treatment of uveitis in the first eye. In 8 patients there was no clinical evidence of syphilis; in 4 there were sparing lesions that characterize a mucocutaneous relapse. The Wassermann reaction was positive in all cases, although in some (cases 2 and 4) it was less strongly positive than in cases of untreated early syphilis.

Case 4 illustrates the possible serious outcome of syphilitic uveitis. The end result was blindness of one eye. The patient had two relapses (iridorecidivism), each occurring after irregular treatment. After retrogression of the nodules and the pupillary exudate, there was destruction of tissue, with cicatrization causing secondary glaucoma.

Group 3.—The 7 patients in this group (6 of whom were Negroes) had positive Wassermann reactions, but clinical evidence diagnostic of syphilis was absent. Four had generalized adenopathy. The history of all gave evidence suggestive of early syphilis (such as a genital lesion, eruption, sore throat), and they were in the age range in which infection more frequently occurs. They had not received antisyphilitic treatment. These patients were among the aforementioned 36 patients with uveitis who were observed for the Herxheimer reaction.[22] This reaction was positive in all the 7 patients, and there was a therapeutic response to antisyphilitic treatment. In view of these considerations and the absence of other causes, these patients are included in the syphilitic group.

RESPONSE TO ANTISYPHILITIC TREATMENT

Chemotherapy: Specific Effect.—In the majority of patients receiving chemotherapy, disappearance of active signs of inflammation, as evaluated by examination with the slit lamp, occurred in from two to five weeks (case 2) and (in exceptional cases) in five to seven weeks (case 1).

One patient received fever therapy, 4 fever bouts preceding chemotherapy. The iritis showed improvement before chemotherapy was instituted. Twenty-two days after onset of fever treatment the affected eye was quiescent; in this interval, in addition to fever therapy, three injections of 0.45 Gm. of neoarsphenamine and one injection of bismuth subsalicylate had been administered.

An equally prompt effect, however, occurred in patients given chemotherapy alone. We see no advantage in fever therapy of syphilitic uveitis except, as aforementioned, to initiate treatment of severe processes, as already discussed. In cases of this type, however, initial reduced doses of a bismuth compound prior to injections of an arsenical serve the same purpose.

It should be emphasized that in treatment of severe inflammation of the anterior uveal tract with complicating processes disappearance of inflammation should be delayed, rather than hastened, in order to avoid, as already discussed, the therapeutic paradox.

22. It is interesting to note that of 36 patients (25 of whom were Negroes) the uveitis of 7 (6 of whom were Negroes), or 19.4 per cent, was regarded as syphilitic.

An important feature of therapeutic response, more diagnostic than the period of retrogression, is prompt improvement after the Herxheimer flare (as aforementioned, this flare-up was absent in 30 per cent of our cases). Subsequent improvement is progressive until inflammation disappears. Failure of the inflammation to subside or its recurrence provided antisyphilitic treatment has been continuous challenges the diagnosis of a syphilitic causation.[23]

Penicillin Therapy—Seventeen patients with uveitis associated with late secondary syphilis were treated exclusively with penicillin, except for local ophthalmologic treatment. Sodium penicillin was employed, the substance being injected intramuscularly every four hours. The total dose was 2,400,000 units, administered in eight days.[24] This period of treatment was exceeded when early doses were more gradually increased. Initial doses, depending on the severity of the inflammatory process, varied from 10,000 to 20,000 units for the first four to six injections, except that for 1 patient with pupillary occlusion and increased ocular tension the initial dose was 5,000 units. Subsequent doses were increased to a maximum of 50,000 to 60,000 units.

Penicillin exerted a prompt effect on the ocular lesion (case 3); inflammation disappeared in from eight to fourteen days after the first injection in all but 2 patients, for whom the latter period was exceeded.

Subsequent to penicillin therapy no further antisyphilitic treatment was administered. No recurrence of ocular inflammation has been observed. The patients are still under observation; the maximum period of observation has been fifteen months. Serologic reactions have become, or are becoming, negative. There was 1 exception; the blood reagin titer decreased after penicillin treatment but subsequently increased. This increase preceded a cutaneous relapse of syphilis ten months after treatment.

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23. After disappearance of the syphilitic uveitis or iritis, the chemotherapy of the syphilitic infection of patients in this study was that recommended for early syphilis—a total of thirty injections of an arsenical preparation and sixty injections of a bismuth compound. The vital importance of continuous treatment (for the first year) should be emphasized to the patient in order to avoid the occurrence of recidivous iritis.

24. It is not to be inferred that this dose and the duration of its administration will finally be accepted as proper for treatment of secondary syphilis. "How best to use it, alone or in combination with other forms of treatment, is as yet undetermined but is under organized, nationwide, governmentally sponsored study, from which definitive results may be expected to emerge" (Moore, J. E.: The Chemotherapy of Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **29**:185-199, 1945). For discussion of treatment and schedules, rate of disappearance of early lesions of syphilis, serologic response and reactions to penicillin, reference should be made to an article by Moore and associates (Moore, J. E.; Mahoney, J. F.; Schwartz, W.; Sternberg, T., and Wood, W. B.: Treatment of Early Syphilis with Penicillin, J. A. M. A. **126**:67-73 [Sept. 9] 1944).

Nonspecific Effect of Antisyphilitic Chemotherapy and Other Treatment.—It is well known that most patients with acute inflammation of the iris and ciliary body respond favorably to fever therapy, foreign protein therapy, administration of salicylates and application of heat and mydriatics. As aforementioned, we observed a beneficial effect of fever on syphilitic iritis. Possek [25] reported on retrogression of syphilitic iritis following fever produced by typhoid vaccine before antisyphilitic treatment was instituted. Musy [26] observed a beneficial effect from injections of sterile milk. Igersheimer [3] stated the opinion that despite the promptness with which syphilitic iritis responds to antisyphilitic treatment it is not to be denied that at times retrogression occurs after simple local treatment, or at least after nonsyphilitic treatment. In this regard, Dianoux [27] reported on the disappearance of syphilitic iritis after local treatment and large doses of acetylsalicylic acid.

The following case illustrates the difficulty in evaluating the significance of a positive Wassermann reaction and a favorable response to antisyphilitic treatment when such treatment had been administered. The patient was in the late stage of syphilis without clinical evidence of the disease. The Wassermann reaction was 4 plus. He had iritis with hypopyon and pupillary exudate. After local treatment, three fever bouts (typhoid vaccine) and extraction of two infected teeth, the inflammatory process retrogressed in two weeks. Visual acuity improved in this time from perception of hand movements at 1 foot (30 cm.) to 6/12. Antisyphilitic treatment was purposely withheld.

Igersheimer [3] further stated the opinion that syphilitic iritis may heal in the absence of treatment. One patient in our series presented himself when iritis of the second eye appeared. The involvement of the first eye had almost disappeared in the absence of any treatment.

Antisyphilitic treatment (arsenicals, mercurials, bismuth, iodides) may exert a nonspecific effect on inflammatory processes of the uveal tract. In 14 patients reported on by Moore [8] who were treated for nonspecific effect of antisyphilitic treatment, improvement as well as retrogression resulted provided treatment was sufficiently prolonged.

Benedict and O'Leary [28] stated the following opinion:

> Treatment for syphilis, including the combined use of arsphenamine, mercury and iodides, has a marked beneficial influence on inflammatory conditions in the uveal

25. Possek, R.: Versuche zur Behandlung luetischer Augenerkrankungen mit unspecifischen Heilmethoden, Wien. klin. Wchnschr. **32**:743-756, 1919.

26. Musy, cited by Stocker, F.: Parenteric Injections of Milk in Eye Diseases, Am. J. Ophth. **3**:58, 1920.

27. Dianoux: Syphilitic Iritis and Aspirin, Clin. opht. **23**:147-148, 1919.

28. Benedict, W. L., and O'Leary, P. A.: The Use of Antispecific Remedies in the Treatment of Diseases of the Uveal Tract, Tr. Pacific Coast Oto-Ophth. Soc. **10**:44-51, 1922.

tract. When these are due to syphilis, the effect is naturally more pronounced than when syphilis is not a factor; but the effect on nonsyphilitic uveitis is none the less gratifying.

They further wrote:

Uveitis occurring in conjunction with tuberculous lesions and tuberculids responds very satisfactorily to treatment for syphilis.

They reported that in 1 patient arsenical and mercurial therapy, given for six weeks, caused retrogression of nonsyphilitic anterior and posterior uveitis. Lucic [29] reported that 10 patients with inflammatory processes of the anterior uveal tract of nonsyphilitic origin responded favorably to neoarsphenamine.

In our experience, the nonspecific effect of antisyphilitic treatment is not uniform. Injections of an arsenical and/or a bismuth preparation may in an occasional patient (case 5) cause disappearance of inflammation of the anterior uveal tract in a manner comparable to the specific effect of such treatment. The nonspecific effect, however, is not always lasting.

COMMENT

It becomes apparent that the Wassermann reaction, the Herxheimer reaction and the therapeutic response to antisyphilitic treatment are not infallible criteria in the diagnosis of syphilitic uveitis. Since a direct diagnosis cannot be made clinically and histologic examination or demonstration of T. pallidum is not possible, diagnosis is essentially made by a positive matching or a negative excluding process. We believe the three most important criteria are: (1) demonstration of, or evidence pointing to, an early stage of the syphilitic infection; (2) an inflammatory process of such character as to exclude as far as is possible other etiologic factors; (3) prompt effect of antisyphilitic treatment.

PROGNOSIS OF SYPHILITIC UVEITIS: FINAL VISUAL ACUITY

Visual acuity after subsidence of the inflammatory process was determined in 50 of the 72 patients. The total number of affected eyes in the 50 patients was 61. Of the 61 eyes, the final visual acuity, in some with correction, in others without correction, was as follows: 6/6, 21 eyes; 6/9, 21 eyes; 6/12 to 6/21, 13 eyes; 6/30, 1 eye; 4/60, 2 eyes; 6/60, 2 eyes; nil, 1 eye. Secondary glaucoma occurred in 3 patients.

The patient who was blinded in one eye (case 4) had vision of 6/9 in the other, previously affected, eye. Another patient who had bilateral involvement had final vision of 6/60 in each eye. At onset of treatment he had pupillary occlusion of both eyes and secondary glaucoma in one

29. Lucic, H.: Neoarsphenamine in the Treatment of Nonsyphilitic Inflammation of the Uveal Tract, Arch. Ophth. **15**:826-832 (May) 1936.

eye. It is to be expected that iridectomy will improve this visual acuity. Excluding this possibility, he is the only patient who is industrially blind. It is apparent from this study that good results are obtained in treatment of syphilitic uveitis (associated with acquired syphilis) and that this form of syphilis of the eye plays a minor role in blindness caused by syphilis.[30]

ILLUSTRATIVE CASES

CASE 1.—*Bilateral iritis; positive Herxheimer reaction; response to antisyphilitic treatment.*

A white man aged 63 when first seen had bilateral plastic iritis of two months' duration. He presented a disappearing macular eruption of syphilis. The Wassermann reaction was 44440. Examination with the slit lamp microscope was made before and after the first injection of neoarsphenamine. For the sake of brevity, only the results of examination of the right eye will be given. Examination before injection of an arsenical disclosed generalized faint haziness of the cornea with wrinkles in Descemet's membrane, and a large number of old and some still active corneal precipitates. The aqueous was slightly turbid and contained several cells. The iris was somewhat dull, and there were no nodules. There were pigment granules on the anterior surface of the lens. Examination eighteen hours after injection of 0.45 Gm. of neoarsphenamine showed an increased haziness of the cornea; the corneal precipitates were more pronounced, and there were more cells in the aqueous. Reexamination forty-five hours after injection of the arsenical showed that the aqueous was slightly clearer and contained only an occasional cell. Examination two weeks later showed decided improvement in the iris. There were no signs of active inflammation on examination five weeks after onset of treatment. In the interval, five injections of 0.45 Gm. of neoarsphenamine had been administered. A soluble bismuth compound was given conjointly with the first two injections of the arsenical.

CASE 2.—*Iridorecidivism; positive Herxheimer reaction and response to antisyphilitic treatment.*

A Negro was first seen January 10 with acute iridocyclitis of the right eye of two weeks' duration. The previous August he had had a chancre and secondary eruption. The Wassermann reaction was 4 plus. He received ten injections of from 0.3 to 0.4 Gm. of neoarsphenamine, until November 18. He then allowed treatment to lapse.

Examination disclosed no evidence of syphilis. The Wassermann reaction was 44000. Examination with the slit lamp microscope sixteen hours after the initial injection of 0.45 Gm. of neoarsphenamine showed that the cornea was more hazed than before injection. There were more debris and corneal precipitates on the posterior surface. The aqueous was more turbid and contained more inflammatory cells. The swelling of the iris was more pronounced. After the patient had received four injections of 0.6 Gm. of neoarsphenamine in the course of twenty-nine days, examination with the slit lamp showed no evidence of inflammation.

CASE 3.—*Therapeutic response to penicillin therapy.*

A Negress aged 21 was first seen May 13 with acute iritis of the right eye of one week's duration and a maculopapular eruption of syphilis of two weeks'

30. This emphasizes the outstanding role of interstitial keratitis and optic nerve atrophy in the generally stated 10 to 15 per cent of all cases of blindness attributable to syphilis.

duration. Dark field examination of material from condylomas on the vulva gave positive results. The Wassermann reaction was 4 plus; the titer was 128.

In addition to local ophthalmic treatment, penicillin (sodium salt) was given intramuscularly every four hours (around the clock) for eight consecutive days. The total dose was 2,400,000 units. The initial doses were purposely reduced to 10,000 units for the first four injections in order to avoid too pronounced a Herxheimer flare; succeeding doses were increased by 10,000 units up to maximum doses of 60,000 and 50,000 units, in order to give the total desired amount in eight days. Three hours after the first injection the patient complained of pain in the affected eye, which soon disappeared.

Examination with the slit lamp microscope was made before and eighteen hours after the first injection. In this interval 60,000 units of penicillin had been administered. The second examination showed more pronounced corneal precipitates than did the first. The aqueous was more turbid and contained a greater number of floating cells. In general, there was more evidence of inflammatory reaction.

Subsequent examinations showed gradual subsidence and complete disappearance of the inflammatory process twelve days after the initial injection. Visual acuity before treatment was 6/9 — 3 and subsequently became 6/6 — 2. Fifteen days after initial treatment other lesions of secondary syphilis disappeared. The titer of the Wassermann reaction was decreased to 32 and still later to 0.

CASE 4.—*Iridorecidivism occurring twice after lapse of treatment, with subsequent blindness in one eye.*

A white man aged 25 was first seen Nov. 20, 1939. He had had a chancre in September 1939, for which he received five intravenous injections. He allowed further treatment to lapse. Two weeks prior to the time we first saw him, the left eye became inflamed, and soon thereafter the right eye was involved.

On his admission there was no evidence of syphilis. The Wassermann reaction of the blood was 32100. The patient presented bilateral iritis. There were nodules on the iris of the right eye, and in the left eye a plastic membrane in the pupillary area was attached to the iris and the lens. Visual acuity was 5/60 in the right eye and was limited to counting fingers at 6 inches (15 cm.) in the left eye.

From Nov. 20, 1939 to Jan. 15, 1940 he received fever therapy—seven intravenous injections of typhoid vaccine and seven weekly injections of neoarsphenamine, 0.45 Gm. He let treatment lapse on Jan. 15, 1940. At that time the right eye was quiescent. There had been a rapid retrogression of the inflammatory process of the left eye; the cornea was faintly hazy. The aqueous was faintly hazed and contained a few inflammatory cells; the iris was markedly disorganized, with atrophy of the entire stroma and posterior synechias; there were opacities of the lens and numerous white opacities in the vitreous.

The patient returned in November 1940. The right eye was normal; visual acuity was 6/9 — 2. The iris of the left eye showed destruction, thinning and atrophy. The pupil was eccentrically oval; there were posterior synechias and a capsular cataract. Intraocular tension was 66 mm. (Schiøtz), and visual acuity was limited to counting fingers. A basal iridectomy was performed. Thereafter the patient attended the clinic regularly, until discharged from antisyphilitic treatment. The final visual acuity of the left eye was nil.

CASE 5.—*Acute anterior uveitis with hemorrhagic retinitis; nonspecific effect of antisyphilitic treatment.*

A Negro was first seen in May 1944 with bilateral uveitis of eighteen days' duration. The previous January he had had a chancre and secondary eruption. The Wassermann reaction of the blood was 4 plus. He thought that he had

received fourteen intravenous injections of neoarsphenamine. He allowed treatment to lapse for the equivalent of three injections, two of which were in consecutive weeks in April.

Examination disclosed no evidence of late secondary syphilis. The Wassermann reaction was 30000. The titer was 1 (in cases of acute untreated secondary syphilis it is about 130). Examination with the slit lamp microscope showed haziness of both corneas with corneal precipitates. The aqueous of both eyes was turbid and contained inflammatory cells. Both irises were dull. There were multiple nodules on the right iris. Broad synechias were present in the right eye, and the lens of this eye was hazed, with numerous opacities of coronary type and considerable pigment on the anterior capsule. There were numerous small exudates in the macular area of each retina and several small scattered hemorrhages. Visual acuity was limited to perception of hand movements in each eye. In addition to local ophthalmic treatment, two injections of a soluble bismuth compound and one injection of 0.3 Gm. of neoarsphenamine were given. Two weeks later examination with the slit lamp showed complete retrogression of the uveitis. Visual acuity was 6/30 in each eye.

The patient returned to the clinic in August 1944. Antisyphilitic treatment had been continuous. Examination (both eyes) with the slit lamp showed slight turbidity of the aqueous and old corneal precipitates and synechias; there was a complicated cataract in the left eye. Ophthalmoscopic examination of the right eye disclosed massive opacities and a dustlike haze in the vitreous; little detail could be seen except that in one peripheral area there was choroiditis with a small hemorrhage. In the left eye only a faint red reflex could be seen. The Mantoux test gave a questionable reaction to tuberculin in a dilution of 0.00002 and a strongly positive reaction in a dilution of 0.0001. Visual acuity was 6/9 in the right eye and was limited to perception of hand movements in the left eye. As the vitreous cleared, more hemorrhages were seen in the vitreous and in the retina, as well as retinitis proliferans. A diagnosis of Eales's disease was then made.

1934 Spruce Street.

1930 Chestnut Street.

RETICULUM CELL SARCOMA OF THE CONJUNCTIVA

ANDREW RADOS, M.D.
NEWARK, N. J.

TUMORS of the hematopoietic system of the conjunctiva are lymphomas, representing an extensive hyperplasia of the lymphoid tissue, either with or without constitutional disease. Tumors of the first type, associated with constitutional disease, are usually unilateral; those of the second type are bilateral and often symmetric. The changes are so well known that it would be pointless to recapitulate the literature. In a second group, the lymphosarcomas, there is evident malignancy; they are clinically soft, rapidly growing tumors and tend to spread through the lymphatics. The histologic appearance approaches that of the benign lymphomas, consisting of small round cells, with occasional larger reticulum cells.

A perusal of the literature dealing with involvement of the lymphatic system shows that as far back as a hundred years ago Hodgkin described a condition affecting the lymph nodes and the spleen. Numerous later investigators delimited distinct entities, such as leukemia and aleukemic leukemia, and Kundrat [1] separated lymphosarcoma from the general group; finally, the terms "reticulosis" and "reticulosarcoma" appeared, characterized histologically by the presence of cells in reticular arrangement.

Lymphosarcoma is distinct from Hodgkin's disease in that it arises in one group of lymph nodes or in any aggregate of lymphoid tissue, spreading to other groups of nodes, is highly malignant and spreads apparently by the way of the lymphatics. It affects males twice as often as females and occurs at almost any age, but more frequently in the fifth and sixth decades of life. Its course is comparatively slow but fatal. The multiple appearance may suggest metastasis, but it probably represents secondary involvement due to widespread operation of the unknown existing cause within the lymphatic system. Lymphosarcoma is a systemic disease; but, according to Boyd,[2] the spread seems to be continuous, while in Hodgkin's disease it is interrupted. Often pro-

From the Ophthalmic Department and Laboratories of the Beth Israel Hospital.

1. Kundrat: Ueber Lymphosarkomatosis, Wien. klin. Wchnschr. **6**:211 and 234, 1893.

2. Boyd, W. A.: Textbook of Pathology, ed. 4, Philadelphia, Lea & Febiger, 1943.

gressive secondary anemia or relative or absolute lymphocytosis occurs; again, an increase of the polymorphonuclear leukocytes may be present. There is a distinct tendency to break through the capsule and invade the surrounding tissues, with fusion of groups of nodes. Necrosis occurs relatively more rarely than in Hodgkin's disease. In lymphosarcoma or malignant lymphocytoma there is complete replacement of the mature lymphocytes with much larger hyperchromatic cells, which have a small amount of basophilic cytoplasm and a round or oval nucleus with fairly prominent nucleolus. The uniformity of the cell type is striking; mitoses are present but are not easy to recognize. The individual cell is distinctly smaller than the cell of reticulum cell sarcoma, and there is no increase of reticulum as seen with silver stains. Only the original content of fibers within the node can be demonstrated, and even the amount seems to be decreased, owing to dispersion by the infiltration of neoplastic cells.

Reticulum cell sarcoma is regarded as a form of lymphosarcoma. Roulet [3] attempted to link up the immature, or reticular, form of lymphosarcomatosis with the sarcomas. He based his conclusions on the concept that lymph nodes possess two types of stroma, the one consisting of fibrous connective tissue, from which the true fibrosarcoma, or spindle cell sarcoma, may be derived, and the other represented by the reticulum cell framework, from which may arise the reticulum cell sarcoma, or "Retothelsarkoma" as he designated it. According to Hallstrom,[4] reticulum cell sarcoma starts with indolent enlargement of the lymph nodes, usually in the upper half of the body. Early, and especially distant, metastasis occurs. The hard consistency of the early stage changes to soft through degeneration in the center. Rapid growth of the tumor with early death is common; in one third of the cases death occurs within the first year. There may be a rise in temperature and anemia, with depression of the red cell count; the leukocyte count usually remains normal; an increase is present in 50 per cent of cases but does not exceed 20,000. In the early stages lymphocytosis, and in the late stages lymphopenia, has been observed. The number of eosinophils and basophils is unchanged; the monocytes occasionally show a slight increase.

If the tumor occurs in the lymph node, often no distinction is made between lymphosarcoma and reticulum cell sarcoma; this is permissible in the case of lymph nodes, the tumor arising from the reticulum cells of the node. But the last decade has taught that the tumor may originate

3. Roulet, F.: Das primäre Retothelsarkom der Lymphknoten, Virchows Arch. f. path. Anat. **277**:15, 1930; Weitere Beiträge zur Kenntnis des Retothelsarkomas der Lymphoknoten und anderer Lymphoiden-Organe, ibid. **286**:702, 1932.

4. Hallström, L.: Retikelzellensarkom unter dem Bilde akuten Strumitis, Chirurg **14**:503, 1942.

in various organs, including bone, where it forms a variety of sarcoma of bone, and therefore the designation of reticulum cell sarcoma seems more appropriate.

The cells of the reticulum cell sarcoma are distinctly larger than those of the lymphosarcoma. The cytoplasm is usually abundant and faintly acidophilic; the nucleus is twice the size of the lymphocyte and is commonly constricted, giving a reniform appearance. Boyd[2] emphasized as highly characteristic the presence of pseudopod-like processes of the cytoplasm and the nucleus, indicating ameboid activity of the living cell. According to Oberling,[5] the tumor is formed by syncytial masses of undivided or slightly fenestrated protoplasm, the limits of which are ill defined, and these masses are connected with zones of more or less differentiated lymphoid tissue. The fenestration, by exaggerating the internuclear spaces, may result in reticular structures. The nuclei, which are round or oval, are irregularly distributed; and the well defined nuclear membrane, sparse chromatin granules and darkly stained nuclear membrane may produce the impression of empty nuclei. Multinucleated cells have been described frequently. The tumor cells often invade the wall of veins, causing constriction or closing of the lumens. The pathognomonic feature, stressed by almost every one, seems to be the distribution of reticulum as seen in silver preparations. In addition to the general increase of reticulum, the argentaffin fibrils exhibit an intimate relationship to the tumor cells, encircling groups of cells and sending fibrils between and around the cells. The picture presented by the silver method demonstrates a variable reticulum, either a dense network or only scattered, delicate fibers. Mitotic figures are frequent. Vascularization is rich, in the form of small vessels, some of them without independent walls. The characteristics are visible only in properly fixed (to prevent distortion by shrinkage) and silver-stained material. The reticulum cell sarcoma is the most undifferentiated form of lymphoid tumors; the masses of syncytial cells reproduce the primitive character of mesenchymal syncytium, with the nuclei keeping their embryonal character. Reference has been made to cases in which reticulum cell sarcoma preceded or accompanied monocytic leukosis.

In order to provide an understandable concept of the changes in proliferation of the cells of the reticuloendothelial system, a primary consideration of the anatomic and physiologic data available cannot be omitted.

The first component of the system to attract attention was the cell designated by Ranvier as the clasmatocyte. He described phagocytosis

5. Oberling, C.: Les réticulosarcomes et les réticulo-endothéliosarcomes de la moelle osseuse (sarcomes d'Ewing), Bull. Assoc. franç. p. l'étude du cancer **17**:259, 1928.

by certain connective tissue elements which were distinct from the ordinary fibroblasts. These phagocytic cells were studied by numerous investigators, each of whom applied a different name to them. In this way, they came to be known variously as macrophages (Metschnikoff), adventitial cells (Marchand), resting wandering cells or polyblasts (Maximow) and, since they play an important role in inflammations, phagocytes. Ribbert [6] was the first to observe their capacity of vital staining with lithium carmine. The application and injection, respectively, of colloidal solutions of acid aniline dyes (trypan blue, pyrrhol blue) intravitally by Goldman [7] proved that certain cells take up the dye in granular form while others do not. Aschoff and Landau, and later Aschoff and Kiyono,[8] popularized the concept of the reticuloendothelial system, which includes all cells which when living are capable of taking up dyes and are therefore phagocytic. These cells include the reticuloendothelial cells proper, the histiocytes and the monocytes.

The reticuloendothelial cells proper are present in hemopoietic organs, i. e., bone marrow, spleen, liver and lymph nodes. They are highly phagocytic, detain foreign particles passing through the organ and take up vital dyes and india ink during life. Ordinarily endothelium of vessels remains unaffected in spite of the circulating solution of the dye. Possibly the germinal cells of lymph nodes belong to this first group of the reticuloendothelial system. The histiocytes, or wandering phagocytic cells of the tissues, the adventitial cells of the vessels, which play important part in the inflammations, form the group of histogenous cells. They are found in all organs, not in the hematopoietic system alone. The monocytes, the last group of the system, are the white blood cells derived from endothelial elements of the reticuloendothelial system. They are important phagocytic cells, known by such diverse names as the large mononuclear and transitional cells of Ehrlich, the endothelial leukocytes of Mallory and the macrophages of Metschnikoff. Before the origin of the monocyte from the reticuloendothelial system was accepted, it was claimed that they came from the lymphocyte (Maximow [9]) or the myeloblast (Naegeli [10]). Quantitatively, the cells are prevalent in the hematopoietic system.

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6. Ribbert, H.: Lehrbuch der speciellen Pathologie und der speciellen pathologischen Anatomie, Leipzig, F. C. W. Vogel, 1902.

7. Goldman, E. E.: Die äussere und innere Sekretion des gesunden und kranken Organismus im Lichte der vitalen Färbung, Beitr. z. klin. Chir. **64**:192, 1909.

8. Aschoff, L., and Kiyono, K.: Zur Frage der grossen Mononukleären, Folia haemat. **15**:383, 1913.

9. Maximow, A. A.: The Macrophages or Histiocytes, in Cowdry, E. V.: Special Cytology, New York, Paul B. Hoeber, Inc., 1932, vol. 2, p. 711.

10. Naegeli, O.: Blutkrankheiten und Blutdiagnostik, ed. 5, Berlin, Julius Springer, 1931.

The function of the cells of the reticuloendothelial system is fourfold: phagocytosis, storage, formation of antibodies and blood production.

The phagocytic activity is obvious, and by virtue of these cells the spleen, liver and lymph nodes are destined to be the great filters of the body, as the iron-bearing pigments of the cells in various diseases clearly testify.

The storage power of the cells is manifested toward lipids, hemoglobin and iron. When lipid as cholesterol is fed to animals for a considerable time or is injected intravenously intra vitam, the cells are filled with the cholesterol. Hyperplasia of cells of the reticuloendothelial system associated with lipidoses belongs in this category. The lipidoses are divided by Thannhauser into cholesterosis (xanthomatosis and Hand-Schüller-Christian disease), cerebrosidosis (Gaucher's disease) and sphingomyelinosis (Niemann-Pick disease, or lipid histiocytosis). The presence of lipids within the cells may be due either to infiltration or to an inherent intracellular disturbance of metabolism within the cells.

The role of the cells in antibody formation was proved through blocking of the cells with india ink or a vital dye, resulting in diminished formation of antibodies.

The role in blood formation includes the production of both red and white cells. Monocytes are formed by proliferation of the special endothelial cells; erythrocytes, by the endothelium of the intrasinusoidal capillaries of the bone marrow. Monocytosis, or increase of the mononuclear cells through stimulation of the reticuloendothelial system, may be observed with malaria, kala azar, brucellosis, endocarditis lenta and some of the septicemias; according to Sabin,[11] they are the precursors of the epithelioid cells in the tubercle.

Soon after delineation of the reticuloendothelial system as a unit, attempts were made to describe the pathologic variations, tumors, whose constituent elements were reminiscent of the newly described system. The reticulum cell sarcoma is the best example of such tumors. Goormaghtigh,[12] in this *reticuloendotheliome*, described the cells of this malignant proliferation as different from the round, mobile elements of the other benign or malignant lymphoid tumors. The term "retothelial sarcoma," introduced by Roulet, has been used to designate a malignant tumor arising in the lymph nodes, the spleen or the bone marrow, and occasionally in the submucosa of the respiratory or the gastrointestinal tract. Possibly Hodgkin's disease may belong to this group; if not a tumor, it is certainly a disorder of this system of cells, a reticuloendotheliosis.

11. Sabin, F. R.: Cellular Reactions to Fractions Isolated from Tubercle Bacilli, Physiol. Rev. **12**:141, 1932.

12. Goormaghtigh, N.: Sur la prolifération maligne du tissu réticuloendothélial des ganglions lymphatiques, Compt. rend. Soc. de biol. **92**:457, 1925.

Ewing [13] suggested first, in 1913, the possibility of tumors arising from the reticulum cells. Roulet [3] proposed the designation *Retothelsarcoma,* the name being shorter than reticuloendothelial sarcoma and more justified, the growth originating not in the endothelial cells of the lymph sinuses but in the cells of the network containing intraplasmic fibrils. Oberling [5] first employed the term "reticulosarcoma" for an immature form of tumor of the bone marrow. Reticulum cell sarcoma does not represent the first stage of tumor formation but is a different form of tumor, originating in well differentiated elements of the tissues. The reticulum, having preserved the original type of mesenchymal cell, offers the possibility of mixed type tumors. Roulet differentiated three types of the tumor: the immature, the mature and the mixed type. In the immature variety the proliferation consists of small cells, 15 to 20 microns in diameter, with almost imperceptible cell contours. The protoplasm contains vacuoles, and often fat droplets. The nuclei are round or oval with chromatin-like dust; delicate particles or granules may be present; differentiation into nucleoli varies according to the maturity of the cells. Neither collagen nor a fibrillary network is visible. Transitional varieties lead from the immature to the mature form. In the latter the proliferating cells show already a pronounced tendency to form nets of argentophile fibers. The cells are polymorphic, large and oval or stellate; they are similar to the cells of the immature form but differ in the presence of short, spindle-shaped cells anastomosing through intraplasmic fibrils. Through amitotic division, giant cells, up to 75 microns in diameter, are produced, the nucleus, large in proportion to the protoplasm, occupying almost the entire cell. The fibrous network consists of parallel stripes; the fibers are thicker than in normal lymph nodes and show a tendency to collagenization. The third, or mixed, variety occurs with leukemia or Hodgkin's disease.

The reticulum cell sarcoma occurs more often in the upper half of the body and is characterized by slow growth and late metastasis or generalized involvement. Roulet had to change his opinion regarding the relatively favorable prognosis on account of the occurrence of the tumors in the abdomen and pharynx and recognized the generalized form. His original opinion that the tumor showed a slighter tendency to metastasis and a generalized form of reticulum cell sarcomatosis than does lymphosarcomatosis was not maintained by his later observations. The reticulum cell sarcoma represents a subdivision in the group of sarcomas originating in the retothelial elements of the lymphatic-lymphoid organs. The metastatic extensions of reticulum cell sarcoma are not confined to the type of tissue in which the primary tumor arose; in contrast, all types of sarcomas of the lymphoid tissue tend predomi-

13. Ewing, J.: Endothelioma of Lymph Nodes, J. M. Research **28**:1, 1913.

nantly to limit themselves to the original type of tissue, that of the hematopoietic system. The true blastomatous nature of lymphosarcomatosis and reticulum cell sarcomatosis seems to be proved, despite the systemic character of the disease, since all the basic criteria of true malignancy are manifested in the growth.

Roulet classified the *Retothelsarkoma* into three and de Oliveira [14] into six types. The types as differentiated by de Oliveira are as follows: 1. The cytoplasmic-syncytial afibrillar type. This is a pure cellular variety, the reticulum cells exhibiting a tendency to free themselves from the syncytial complex but remaining connected with the syncytium through thick cellular projections. Fibrils are absent in silver preparation. 2. The type characterized by a tendency to isolation of cells and appearance of intraplasmic argentophile fibers. 3. The fibroreticular-syncytial form, stellate cells forming syncytial nets, with well defined cell contours and pronounced reticular nets of silver-impregnated fibrils. 4. The fibrocellular form, corresponding to the mature stage of reticulum of the lymph nodes. The cells are not connected through syncytial elements but are joined by delicate projections or are free on the network. Numerous fibrils appear in silver preparations, projecting in all directions and encircling the cells, thus producing an alveolar appearance. 5. The form characterized by polymorphic cells with giant cells. 6. The type with differentiation in a hematopoietic direction. According to the dominance of lymphoid or myeloid elements, tumors of the last type are called reticulum cell lymphosarcoma and reticulum cell myelosarcoma. De Oliveira emphasized the tendency to the generalized form of the tumors and the malignant character. There is a predilection for the upper half of the body, but the tumor is often encountered in the abdomen, and in the latter case is even more malignant. The prognosis was given as unfavorable, death occurring within a comparatively short period.

The classifications of Roulet and de Oliveira are widely used, but before the work of these authors, soon after Aschoff's delineation of the reticuloendothelial system as a physiologic unit, attempts were made to describe the pathologic variations, tumors whose constituent cells were reminiscent of the elements of the sharply demarcated new system. Oberling and Oberling and Raileanu [15] applied the designation *réticulosarcome,* Parker and Jackson,[16] in this country, that of reticulum cell sarcoma. The classification of the Lymphatic Tumor Registry defines

14. de Oliveira, G.: Ueber die Stellung der Retothelsarcome im System der Lymphdrüsengeschwülste, Virchows Arch. f. path. Anat. **298**:414, 1936.

15. Oberling, C., and Raileanu, C.: Nouvelles recherches sur les réticulosarcomes de la moelle osseuse (sarcomes d'Ewing), Bull. Assoc. franç. p. l'étude du cancer **21**:333, 1932.

16. Parker, F., Jr., and Jackson, H., Jr.: Primary Reticulum Cell Sarcoma of Bone, Surg., Gynec. & Obst. **68**:45, 1939.

reticulum cell sarcoma as a malignant tumor of reticulocytes (monocytes) and implies its close relation to the sarcomatous form of Hodgkin's disease. The reticulum cell sarcoma represents the most undifferentiated form of lymphoid tumors. According to Warren and Picena's [17] concept, the lymphoid tissue is a network of undifferentiated cellular reticulum (stem tissue), with lymphoid cells (lymphoblasts, prolymphocytes and lymphocytes) embedded in the interstices. Malignant tumors may originate in the reticulum of the lymphocytic or lymphoblastic cells, or they may be mixed, a combination in which reticulum and lymphoid cells are affected. Gloggengiesser [18] held that the localization, cause, prognosis and histologic structure justify the differentiation of the tumors originating in the reticulum cells from the lymphosarcomas and endothelial sarcomas, the former exhibiting the tendency to generalized appearance and infaust prognosis.

Verhagen,[19] in 1940, tabulated 64 cases (31 male, 33 female), including his own. In the early stages, according to his description, the lymph nodes are very hard but painless. The tumor may originate in any lymph node and remains for a relatively long time limited to one group of nodes; later, infiltrative progress may be noticeable but is less frequent in the generalized form. Pain is due to compression of nerves or vessels of the neighboring structures. Most of the clinical symptoms are referable to the space-occupying quality or mechanical interference of the growth, but the progressive loss of weight, leading to typical cachexia, indicates the malignant nature. The progress is rapid; of 35 patients, 8 died within three months, 7 in less than nine months, 6 within one year and 11 in less than four years. The lymph nodes of the neck, axillas, tonsils and pharynx appear to be sites of predilection. The growth is most probably of multicentric origin. Primary origin in the lower half of the body prevails in females. In 50 per cent of the cases generalized involvement of all lymph nodes occurred, with the presence or absence of organ metastasis about equally distributed. Metastases frequently were found in the liver and spleen, less frequently in the lungs, kidney, adrenals and heart; they were more often encountered in the bones, especially in the spine. Metastasis was rare in the gastrointestinal tract, the brain and the uterus. The route of spread is the lymphatic vessels, but possibly the blood vessels are

17. Warren, S., and Picena, J. P.: Reticulum Cell Sarcoma of Lymph Nodes, Am. J. Path. **17**:385, 1941.

18. Gloggengiesser, W.: Generalisierte Retothelsarkomatose, Virchows Arch. f. path. Anat. **306**:506, 1940.

19. Verhagen, A.: Ueber das Retothelsarkom in seiner histologischen und klinischen Bedeutung, Ztschr. f. Krebsforsch. **50**:163, 1940. Benecke, E.: Ueber leukämische Myeloretikulose mit Uebergang in Retothelsarkom, Virchows Arch. f. path. Anat. **306**:491, 1940.

instrumental. Increase in temperature is part of the picture, not only in the generalized but in the localized variety of the growth. Secondary anemia is almost a constant feature, the erythrocyte count sinks to from 3,800,000 to 2,800,000; the white cell count approached normal figures only in 9 cases, being below 5,400 in 9 cases and from 8,000 to 20,000 in 18 cases. In 13 cases increase of neutrophils was noted, with slight or moderate lymphopenia. In the beginning the reticulum cell sarcoma responds to radiation, which gives place in a short time to renewed swelling of the original or other sites, of radiation-resistant character. The primary tumor and the metastases may differ in degree of differentiation; all varieties, from the immature sarcoma to the more mature structure, with argentophile fibers and a network of fibrils, and finally, the almost mature type, with differentiation of the tumor cells in the hematopoietic direction, are occasionally represented in the same case.

The formation of tumor occurs in all sites of physiologic location of lymphoid tissue and is therefore almost ubiquitous; the lymph nodes, the bone marrow and the respiratory, digestive and urogenital tracts may be the site of origin. Oberling first described the growth in bones; according to Szutu and Hsieh,[20] the tumors of bone metastasize relatively late, in contradistinction to reticulum cell sarcomas of the soft tissues, in which the generalized spread occurs relatively early. Kinney and Adams [21] described 3 cases of primary reticulum cell sarcoma of the temporal lobe of the brain. The cells of the tumor resembled and had common origin with the histiocytes, and the reticulum was formed by fibroblasts stimulated to activity by the tumor cells. Owing to the fact that the histiocyte is found in any organ of the body, the tumor was described as originating, among other sites, in the thoracic wall, the thyroid, the ovary and the testis. Kirshbaum, Larkin and Culver [22] designated the prostate as the site of origin. These authors called attention to the opinion expressed by Ewing [13] that the normal gland does not contain adenoid tissue and, consequently, that the lymphosarcoma must be explained as anaplastic carcinoma. Conversely, Symmers [23] stated the belief that the prostate gland belongs to the auxiliary lymphatic system, containing interstitial lymphoid foci, and Wegelin [24] maintained that in certain organs (skin, thyroid, kidney and

20. Szutu, C., and Hsieh, C. K.: Primary Reticulum Cell Sarcoma of Bone: Report of Two Cases with Bone Regeneration Following Roentgenotherapy, Ann. Surg. **115**:280, 1942.

21. Kinney, T. D., and Adams, R. D.: Reticulum Cell Sarcoma of Brain Arch. Neurol. & Psychiat. **50**:552 (Nov.) 1943.

22. Kirshbaum, J. D.; Larkin, H. S., and Culver, A.: Retothel Sarcoma of Prostate Gland, J. Urol. **50**:597, 1943.

23. Symmers, D.: Primary Lymphosarcoma of Prostate, Arch. Surg. **6**:755 (May) 1923.

prostate gland) lymph follicles, although normally absent, may evolve as part of the inflammatory reaction. Jenney [25] observed reticulum cell sarcoma occurring spontaneously in the mesenteric lymph nodes of albino rats; the tumor was successfully transferred through twelve passages by subcutaneous implantation into animals of the same strain. The constituent cells were pleomorphic, being composed of large cells with a moderate amount of cytoplasm and large clear nuclei with one or two prominent nucleoli. Similar, but much larger, cells with two or three nucleoli were present as well as small lymphoid cells. The characteristic reticulum was composed of branching fibrils of varying thickness, distributed among the cells. Tumor transfers not only invaded the adjacent muscle tissue but led to distant metastases in the lung, liver, spleen, mediastinum, kidney and bone marrow. The inoculated tumors grew commonly more expansively than did the spontaneous variety.

The reticulum cell sarcoma shows a predilection to arise in the upper half of the body, but the unusual location of the primary tumor in tissues of the palpebral conjunctiva and the subsequent rapid expansion and death of the patient present unusual and interesting features. It seems that the case I am about to describe is the first one of its kind in the ophthalmologic literature; careful search did not reveal any other observation that could be correlated with mine.

REPORT OF A CASE

Past History.—A. L., a white man aged 29, six months before admission had had an incision made on the left lower lid because of a "blood clot."

Family History.—The family history in general was noncontributory.

Laboratory Data.—The urine was clear and alkaline in reaction, and the specific gravity was 1.020. Occasional epithelial casts and triple phosphate crystals were noted.

The leukocyte count was 12,000, with 69 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes and 2 per cent endothelial leukocytes; the hemoglobin concentration was 108 per cent, and the erythrocyte count was 5,000,000.

The Wassermann, Kline, Frei and Mantoux tests gave negative reactions.

The evidence of gross pathologic change on roentgenographic examination of the thorax was insufficient to be of diagnostic value.

Clinical Examination.—Left Eye: There was marked ptosis of the upper lid, without redness or edema. As compared with the normal (right) palpebral fissure, the left was two thirds closed. There was no pain or tenderness around the orbital margins.

The everted conjunctiva of the upper lid exhibited numerous large papillary hypertrophies. The papillae were red and seemed of firm consistency; touching them did not produce any bleeding. These papillary hypertrophies were similar

24. Wegelin, C.: Ueber ein Lymphom der Prostata, Wien. klin. Wchnschr. **48**: 1236, 1935.

25. Jenney, F. S.: Reticulum Cell Sarcoma of Rat Transferred Through Twelve Successive Passages in Animals of Related Stock, Cancer Research **1**:407, 1941.

to those seen in cases of severe vernal conjunctivitis; however, they were unilateral, were present on the palpebral conjunctiva of the upper and lower lids and were much larger than are ever observed with conjunctivitis vernalis. The conjunctiva of the lower lid was equally covered with papillary hypertrophies, and in the lower fornix there was a pea-sized, round tumor-like mass.

Lymph Nodes: The right preauricular lymph node was the size of a lima bean, without inflammatory symptoms; it caused conspicuous bulging of the skin, which was freely movable. Neither spontaneous tenderness nor pain on pressure could be elicited. There were slightly enlarged lymph nodes on both sides of the neck.

Treatment and Course.—The clinical picture was a rare one indeed, and biopsy of the conjunctival mass was performed, followed a few days later by excision of the enlarged left preauricular lymph node.

After the biopsy, the left eye and the left preauricular region were subjected to roentgen irradiation, on Nov. 11, 1943 the patient receiving 200 r to the left eye and on November 12, 150 r each to the left eye and the left preauricular region; the same dose was given again to both areas the next day (November 13).

The patient was readmitted to the hospital on March 3, 1944.

Immediately after exposure to roentgen radiation the patient had complete closure of the lids; the upper and lower lids showed enormous swelling and redness. Eversion of the upper lid became impossible; the conjunctiva of the upper lid could not be seen; the hypertrophic projections of the lower lid showed definite retrogression. The preauricular region was normal and the scar of the incision almost imperceptible. The patient complained of excruciating pain in the back, but the physical, neurologic and roentgenologic examinations revealed nothing significant.

On March 21, 1944, the patient was discharged, with his condition unimproved.

He was readmitted three days later on account of unbearable pain in the lower part of the back.

The urine was cloudy and alkaline in reaction, and the specific gravity was 1.010.

The leukocytes numbered 3,300, with 79 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes; the hemoglobin concentration was 48 per cent and the erythrocyte count was 2,310,000.

In order to relieve the pain, a 1 per cent solution of procaine hydrochloride was repeatedly injected into the painful areas, and the right posterior and pelvic regions each received eleven treatments, between March 31 and April 17, 1944, with 150 r of high voltage roentgen radiation, without any relief. Codeine could not control the pain.

About April 1 a septic temperature developed; on April 17 a systolic murmur wa noted in the mitral area; on April 19 the formerly negative roentgenogram of the chest showed loss to absence of illumination over the lower third of the left pulmonic field and areas of rarefaction at the interior angle of the right scapula. The diagnosis (Dr. J. Furst) was probable neoplastic metastasis. The septic temperature continued; repeated blood cultures yielded no pathogens. On medical consultation, on April 25, no clinical signs were found in the chest. The blood picture showed 3,300 leukocytes, with 79 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes; 2,310,000 erythrocytes, and 48 per cent hemoglobin. The patient had marked tachycardia with a systolic blowing sound. The possibility of osteomyelitis with discharge of septic emboli into the blood stream was suggested. On May 5 the patient showed striking euphoria. Neurologic examination revealed definite signs of multilocular impairment of the spinal cord, muscular atrophy of the middle part of the right hand, a bilateral Hoffmann sign and absence of abdominal reflexes. Only slight active movement was present in

the left leg; the right leg was completely paralyzed. The muscles of the legs were flabby; the knee and ankle jerks were hyperactive. There was evident ankle clonus, which was persistent on the left side and abortive on the right. A Babinski sign was elicited on the right. There were marked hypalgesia from the toes to the ninth dorsal segment and hyperesthesia to touch. Position sense was absent in the toes of the left foot and decreased in the toes of the right foot. Vibration sense was absent in the left foot and diminished in the right foot. The neurologic changes indicated metastasis in the cervical and dorsal portions of the spinal cord, involving the anterior horn, the pyramidal tracts and the posterior columns.

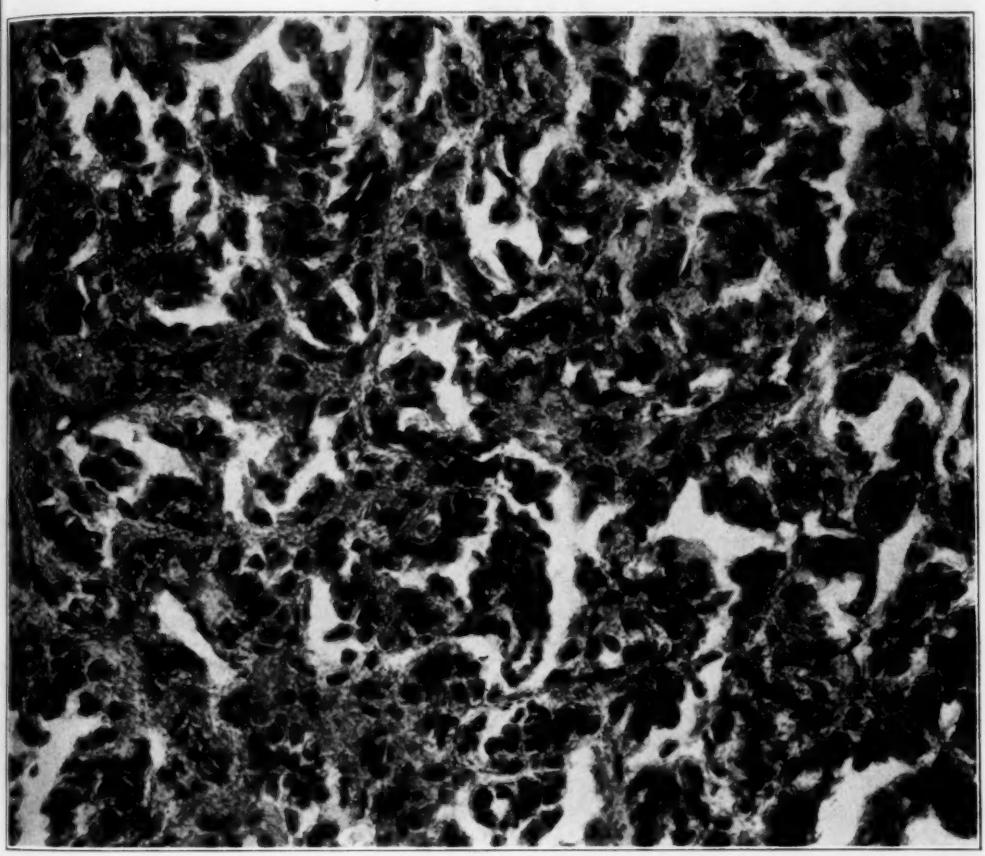

Fig. 1.—Section through a tumor showing the medullary character, large cells with ample cytoplasm and highly cellular structure.

The patient's pain could not be relieved; on May 10 he began to fail rapidly and was kept under sedation with large doses of morphine; he died on May 18, 1944.

Histologic Study.—The section of the conjunctival tumor and that of the preauricular lymph node showed the same medullary tumor tissue, consisting of large cells with ample cytoplasm and highly polymorphoric nuclei. The cells were uniform in shape and size. Round and oval vesicular nuclei alternated; the chromatin was fine and widely dispersed. Some of the cells were exceedingly

large and resembled somewhat the giant cells of Hodgkin's disease. This resemblance is not surprising in view of the origin of both cells from the reticulum cells. Few mitotic figures were discernible; vascularity was rich. The cytoplasm of the smaller cells was variable in quantity and occasionally showed pseudopods, indicating ameboid activity. The origin of the cells was substantiated by the silver impregnation, which revealed close contact between the cells and the argentaffin fibrils. These fibrils not only surrounded large cell groups with a

Fig. 2.—Section from the same specimen with silver staining, exhibiting the rich texture of argentaffin fibers, the characteristic feature of reticulum sarcomas. × 465.

ringlike structure but permeated the cell groups coming into close contact with the individual cells.

A similar relation between the parenchyma of the tumor and the reticulum is the property only of tumors arising from the fibril-producing elements. In other tumors, particularly carcinomas, the argentaffin fibrils remain outside the

parenchyma or penetrate the latter only where strands of connective tissue on blood vessels carry reticulum cells along. No such fibrils enter between the individual cells. In this case the strands formed a network, constituting the stroma. The highly cellular character of the tissue and its great polymorphism are indicative of the malignant tendency.

The unilateral growth, which originated in the upper and the lower palpebral conjunctiva, appeared as extremely large papillary hypertrophies and were of firm consistency. The preauricular node and the lymph nodes of the neck were enlarged and palpable. About five months later the patient experienced unbearable pain in the back, had a septic temperature with a sterile blood culture and died about seven months after the tumor appeared on the conjunctiva, with symptoms suggestive of multilocular metastases in the spine.

COMMENT

The ophthalmologic literature reveals 2 cases of a conjunctival tumor diagnosed as reticulum cell sarcoma. But in both cases the tumor was local, without the systemic involvement characteristic of reticulum cell sarcoma. The first case, reported by Siotto,[26] was that of a girl aged 17 years. The red cell count was 4,500,000; the hemoglobin concentration 70 per cent and the white cell count 6,500 with 65 per cent neutrophils, 1 per cent eosinophils, 32 per cent lymphocytes and 20 per cent monocytes. There was enlargement only of the submandibular lymph node, and the patient was free of symptoms after removal of the growth and irradiation and remained so at the time of examination, six months later. The second case, reported by Black,[27] was that of a man aged 67, in which a dark, plum-colored tumor of primary type was attached by fibrous trabeculae to the external rectus muscle. The bulk of the tumor consisted of large, closely packed cells, with round or oval vesicular nuclei and ill defined cytoplasm, and the characteristic reticulum cells. However, staining for reticulum was not reported on, and generalized symptoms were missing, as they were in the case of Siotti. The lack of such generalized manifestations in both cases leaves the classification of the tumor as a reticulum cell sarcoma a moot question, to say the least. The reticulum cell sarcoma may occur at all sites of physiologic location of lymphoid tissue and does not spread by metastasis from the site of the first clinical manifestation but, rather, spreads by systemic involvement of the entire system, which was so evident in our case that it eliminated the element of doubt and the need of further investigation.

The sarcomas consisting of reticulum cells are tumors of rapid growth and of highly invasive type, localized occasionally in the begin-

26. Siotto, G.: Contributo alla conoscenza del reticuloma della congiuntiva (osservazione clinico-istologica), Rassegna ital. d'ottal. **9**:477, 1940.

27. Black, G.: Reticulum Cell Sarcoma, Tr. Ophth. Soc. U. Kingdom **62**:316, 1943.

ning but spreading locally and along the lymph vessels and often setting up distant, blood-borne, metastases. The most usual sites of origin are the lymph nodes, liver, bone marrow and respiratory, digestive and urogenital tract, but occasionally the growth may arise in any other organ containing lymph tissue elements. The growth represents the malignant proliferation of the cells of the reticuloendothelial system of varying degrees of maturity, with the outstanding characteristic of proliferation of the argyrophilic reticulum.

Consideration of the normal anatomic relations and the histologic structure of the conjunctiva furnishes ample proof that tumors may originate occasionally primarily in the conjunctiva. The subepithelial accumulation of lymphocytes and plasma cells is absent in the newborn, but beginning with the third month lymphocytic infiltration and small nodules are visible, especially in the upper fornix. The normal conjunctiva shows a prominent subepithelial follicle-like accumulation of small lymphoid cells in the tarsal portion, the number diminishing toward the bulbar portion of the conjunctiva. The reticuloendothelial system is well represented in the conjunctiva. I [28] was the first in the ophthalmologic literature to report, in 1913, on an extensive study of this system in the eye. Vital staining with lithium carmine, pyrrhol blue and trypan blue was employed, and the presence of the vitally stained cells under normal and inflammatory conditions was considered. The clasmatocytes were found in large numbers not only in the palpebral but in the bulbar part of the conjunctiva; at the latter site even a large accumulation was noted. In the subepithelial adenoid layer of the palpebral conjunctiva the clasmatocytes were mixed with the lymphoid elements. My observations were later confirmed by numerous other authors, among them Schnaudigel, Löhlein and Albrich, and the presence of these cells constitutes a generally accepted and proved histologic feature of the conjunctiva. Aschoff and Kiyono, in 1913, introduced the term histiocyte to designate the mesenchymal mononuclear phagocyte and popularized the concept of the reticuloendothelial system. The fact that the conjunctiva under normal conditions contains both lymphoid tissue and elements of the reticuloendothelial system constitutes the basis of malignant proliferation; primary tumors arising in the conjunctiva spread through this system in the same way as do the malignant growths of the same type arising in the lymph nodes.

31 Lincoln Park.

28. Rados, A.: Die Ausscheidung von intravenös injiziertem Carmin und Trypanblau im Auge, Arch. f. Ophth. **85**:381, 1913; Ueber die vitale Färbbarkeit der Endothelien der Descemetschen Membran, Klin. Monatsbl. f. Augenh. **17**:421, 1914.

AQUEOUS FIBRIN FIXATION OF CORNEAL TRANSPLANTS IN THE RABBIT

HERBERT M. KATZIN, M.D.
NEW YORK

PUBLISHED reports of the use of fibrin as a substitute for sutures aroused my interest in the possibility that this material might be used in corneal grafting. The use of plasma proteins in surgery has been greatly expanded under the impetus of the recent war, particularly since the Harvard Physical Chemical Laboratories had been commissioned to study the fractionation of human blood plasma. A great many uses have been developed from the fibrinogen fraction, which is the biologic plastic cement substance of the blood.

Fibrinogen molecules are long and narrow and become oriented in parallel in a fast flowing stream.[1] When a clot is formed, these molecules form a meshwork pattern. The mechanism of clotting is believed to be brought about by the action of thrombin on fibrinogen.[2] Thrombin exists in the blood plasma as prothrombin and is transformed into thrombin in the presence of calcium ions by thromboplastins. These thromboplastins are liberated from injured tissue cells. Traces of thrombin in the blood are neutralized by antithrombins, and fibrinolytic enzymes are present in the plasma which dissolve fibrin clots after a variable period. There are also certain chemical agents which can prevent clotting, such as heparin, which is believed to inhibit the formation of thrombin from prothrombin, and hirudin, which prevents the action of thrombin on fibrinogen.[3]

This work was done under a grant from the Ayer Foundation.

From the Corneal Research Laboratory of the Manhattan Eye, Ear and Throat Hospital.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, May 21, 1945.

1. Cohn, E. J.; Oncley, J. L.; Strong, L. E.; Hughes, W. L., Jr., and Armstrong, S. H., Jr.: The Characterization of the Protein Fractions of Human Plasma, J. Clin. Investigation **23**:417-432, 1944.

2. Edsall, J. T.; Ferry, R. M., and Armstrong, S. H., Jr.: The Proteins Concerned in the Blood Coagulation Mechanism, J. Clin. Investigation **23**:557-564, 1944.

3. Howell, W. H.: Textbook of Physiology for Medical Students and Physicians, ed. 12, Philadelphia, W. B. Saunders Company, 1933, p. 486.

The Harvard group has processed fibrinogen into a number of forms, such as fibrin foam, films and plastics,[4] which have been used in the solution of a great many surgical problems. This material has been used as a protective agent in the surface treatment of burns,[5] as an aid in the operative removal of renal calculi[6] and as a hemostatic agent in neurosurgery[7]; it has also been employed to repair dural defects,[8] to hold skin grafts in position,[9] to aid in reconstructive surgery[10] and to cement together the severed ends of peripheral nerves.[11]

The adhesive action of natural fibrin has also been recognized in various operations about the eye, but in order to form fibrin blood vessels must be severed. Since human aqueous contains only traces of fibrinogen[12] and since the cornea is avascular, there is no natural source for fibrinogen in corneal surgery. The aqueous that regenerates after a paracentesis on the human eye contains slightly larger amounts of fibrinogen. In animal eyes, however, the protein content is much increased after paracentesis.[13] In rabbits the regenerated aqueous contains such a large amount of fibrinogen that a clot forms within several minutes of the time the anterior chamber has been opened. This property of rabbit aqueous in relation to healing of corneal wounds was studied by Brown and Nantz.[14] These authors prepared corneal trans-

4. Ferry, J. D., and Morrison, P. R.: Fibrin Clots, Fibrin Films and Fibrinogen Plastics, J. Clin. Investigation **23**:566-571, 1944.

5. Hawn, C. Z.; Bering, E. A., Jr.; Bailey, O. T., and Armstrong, S. H., Jr.: A Note on the Use of Fibrinogen and Thrombin in the Surface Treatment of Burns, J. Clin. Investigation **23**:580-585, 1944.

6. Dees, J. E.: Fibrinogen Coagulum as an Aid in the Operative Removal of Renal Calculi, J. Clin. Investigation **23**:576-579, 1944.

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8. Bailey, O. T., and Ingraham, F. D.: Fibrin Films in Neurosurgery, with Special Reference to Their Use in the Repair of Dural Defects and in the Prevention of Meningocerebral Adhesions, J. Clin. Investigation **23**:597-600, 1944.

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12. Hayano: Ueber die Fermente in Kammerwasser, in Festschrift für Prof. Komoto, abstracted, Klin. Monatsbl. f. Augenh. **65**:755, 1920.

13. Hagen, S.: Weitere Untersuchungen über die Regeneration des Kammerwassers im menschlichen Auge, Klin. Monatsbl. f. Augenh. **66**:493-507, 1921.

plants 4 to 5 mm. in diameter by means of a small cataract knife. A traction suture was inserted in the center of the corneal apex before the transplant was incised. The transplant was replaced in situ after it had been detached, and fibrin was allowed to form to cement the graft in place. At various intervals the traction necessary to separate the graft from its bed was measured and after four hours was found to be 11,000 times the weight of the graft.

The problem which was studied was the use of fibrin as a complete substitute for sutures in performing corneal grafting operations in the rabbit.

METHOD

Since the operation requires about twenty minutes to perform, it was necessary to prevent the premature formation of fibrin clots. This was done by the intravenous injection of heparin. In a 2 Kg. rabbit, 5 mg. of heparin prevents

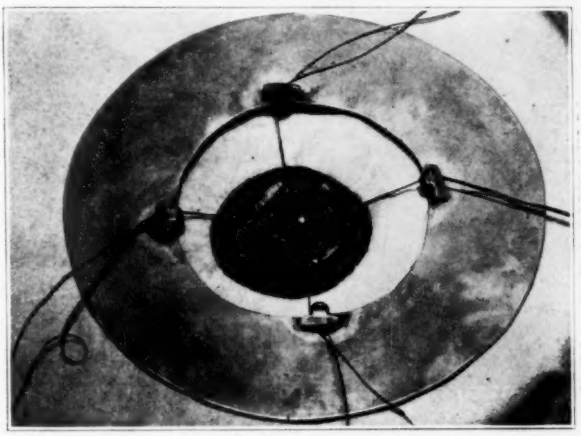

Fig. 1.—The sutures are passed through the superficial layers of the limbus and wound around cleats on the aluminum disk. No speculum is necessary, as the sutures hold the lids out of the way.

aqueous clotting for thirty minutes. To reverse the action of heparin, Hemostatic Globulin (Lederle) was used locally. This material is prepared from rabbit plasma and contains the thrombin fraction.[15]

The rabbits were given a basal anesthesia by intravenous administration of sodium pentobarbital, supplemented by the injection of 4 per cent procaine hydrochloride into the lids and behind the eyeball. The eye was fixed by four sutures passed through the limbus and tied to an aluminum disk provided with cleats. A central suture was placed in the cornea and a 4.5 mm. disk removed with trephine and scissors. The disk was replaced temporarily while a graft was removed with

14. Brown, A. L., and Nantz, F. A.: Corneal Healing: The Adhesive Power of Aqueous Fibrin in the Rabbit; Preliminary Report, Am. J. Ophth. **27**:1220-1224, 1944.

15. Parfentjev, I. A.: A Globulin-Fraction in Rabbit's Plasma Possessing a Strong Clotting Quality, Am. J. M. Sc. **202**:578-584, 1941.

the same trephine from a donor rabbit's eye. Then the excised disk was lifted from the recipient eye, 1 minim (0.065 Gm.) of Hemostatic Globulin dropped into the anterior chamber and the graft placed in situ. Another minim of the globulin was placed on top of the graft; a drop of a 3 per cent solution of atropine sulfate was instilled, and the lids were sutured with three intramarginal sutures.

For the first five postoperative days the rabbit was left untouched. Then the lid sutures were removed, and atropine was instilled daily.

COMMENT

Large amounts of fibrin begin to form as soon as the globulin is introduced, and the transplant must be placed in its bed promptly and with care so that its position does not have to be shifted. A layer of fibrin also forms on top of the cornea, precipitated from the released aqueous. With a well fitted graft, the anterior chamber will fill rapidly and reform under observation. At the time the lid sutures are removed

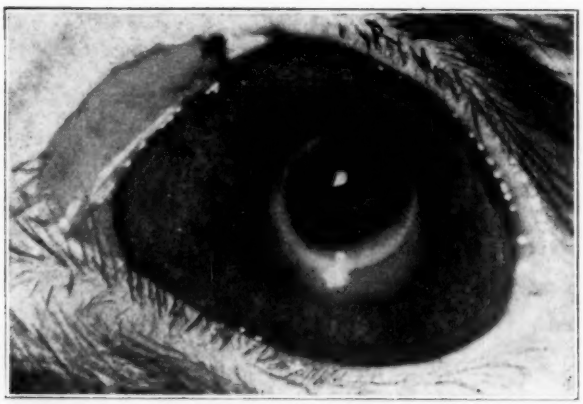

Fig. 2.—A clear graft three weeks after operation.

the graft is usually hazy, as a result of interstitial edema. This haziness requires one to two weeks to clear.

The use of rabbits for this experiment has imposed several obstacles which do not exist with the human subject. The exposed position of the rabbit eye and our inability to maintain immobilization of the animal during the postoperative course have predisposed to accidents which are avoided in the human subject. Also, the operation is technically more difficult in the rabbit because of the softer consistency of the cornea. Several authors have reported the performance of the grafting operation in human eyes without the use of sutures, but with indifferent success.[16] To apply the fibrin fixation method to human subjects, both fibrinogen solution and thrombin would have to be added.

16. Gradle, H. S.: The Present Status of Keratoplasty, Am. J. Ophth. **4**:895-899, 1921. Thomas, J. W.: Transplantation of Cornea, Tr. Ophth. Soc. U. Kingdom **50**:127-141, 1930.

RESULTS

This procedure was applied to corneal transplantation in 37 rabbits. In 32 of these animals the graft held and healed in position. In 5 rabbits the graft slipped; in 1 of these there was gross infection. The transplants remained clear for periods up to six months in 18 rabbits and became opaque in 14 rabbits.

SUMMARY AND CONCLUSION

Corneal grafts were performed in rabbits, using the fibrin formed in the anterior chamber as the only fixing agent. The technic used is described, and the procedure was performed in 37 eyes. The grafts held in 86 per cent and remained clear in 48 per cent of the eyes. We hope soon to be able to use fibrin in a similar manner in operations on the human eye.

We believe that there is great significance in the successful use of fibrin to hold corneal grafts in place during healing. The significance is great not only because the operation itself may be vastly simplified thereby but because the corneal graft is an ideal test medium for wound healing of all types. The area of contact between graft and host, after the anterior chamber has reformed, is of very small dimensions. Also, the tissue reaction to the fixing agent is immediately apparent in the transparency of the corneal graft.

1148 Fifth Avenue.

DISCUSSION

DR. R. TOWNLEY PATON, New York: Dr. Katzin has demonstrated that the aqueous fibrin fixation of corneal transplants is possible in rabbits. A similar method has been applied to the human eye in 1 case. It was not deemed safe to eliminate the sutures to hold the transplant in place. It was noted, however, that the anterior chamber refilled immediately as the fibrin was dropped on the cornea. Also, it seems that the fibrin acts somewhat as a protective dressing. I hardly think that in operations on the human eye sutures will be entirely eliminated; but the application of fibrin will act as a reenforcement to keep the graft in place, and the fibrin, when injected into the anterior chamber, will act as a cushion and a protection to the lens.

DR. RAMON CASTROVIEJO, New York: One will have to wait until a method of applying fibrin to hold corneal transplants in place has been used extensively in order to be able to state whether such a method will be of practical value. From the experience gained in cataract surgery, it may be assumed that holding the transplant in the cornea of the host will have to be accomplished by the same methods as those used for closing the incision in cataract extractions. In cataract extrac-

tions the incision was first left to cicatrize without sutures; then, to prevent prolapse of the iris and other postoperative complications, conjunctival sutures were used, and recently corneoscleral sutures, which close the incision more firmly, are favored by many ophthalmic surgeons.

I believe it will be found that the best suture is that which will keep the graft in the eye of the host more securely in place, without danger of prolapse.

Dr. R. Townley Paton gave help and guidance and Miss Florence Schorske and Mrs. Fannie Gruber technical assistance in this work.

Clinical Notes

CONJUNCTIVITIS AND DERMATITIS DUE TO "BEACH APPLE"

Report of Thirteen Cases

CAPTAIN PHILIP C. GRANA, MEDICAL CORPS, ARMY OF THE UNITED STATES

IN 1942, in Panama 13 cases of acute conjunctivitis and dermatitis were observed and attributed to an agent which, so far as could be determined, had not previously been reported in a large number of cases.

During maneuvers of an infantry regiment one company took up defensive positions along a stretch of Pacific Ocean beach at night. The men dug foxholes and then proceeded to camouflage them by utilizing pieces of shrub found in the vicinity. This is in accordance with good military practice, as it affords a disguise which conforms with the surrounding terrain. It so happened that "beach apple" plant was easily accessible, and hence it was used.

The scientific name of the plant is Hippomane manchinella L. (Euphorbiaceae). The common names in current use are "manzanillo" and "beach apple." It is described as a gray-barked, round-topped tree found on the seabeaches of the West Indies and Central America. The small green fruit resembles a crab apple and, if eaten, sometimes causes death.[1]

Not more than two hours after the men dug in on the beaches, 3 casualties were brought to the clearing station. The history was essentially the same in all 3 cases; the men had used "beach apple" for camouflage and had inadvertently touched their eyes. The chief complaints consisted of excrutiating pain referable to the orbital contents, intense photophobia, blurring of vision and profuse lacrimation.

Examination revealed pronounced swelling of the lids, associated with redness. The palpebral and bulbar conjunctivas were intensely injected in a diffuse fashion, and there was some slight evidence of chemosis. Tearing was pronounced. A more detailed study of the eyes could not be performed, owing to inadequate facilities. Furthermore, the patients resisted prolonged exposure of the eye for examination because of the intense pain and photophobia.

In addition to the eye, the skin of the face showed a diffuse, patchy erythema and swelling. Subsequently, 10 additional casualties arrived in a group at the clearing station. The history was the same as that previously elicited except that several of the soldiers denied any direct contact with "beach apple"; yet the lesions observed were similar to those of the men who had touched the plant. They did state, however, that they were in the vicinity of the plants but were engrossed in duties other than camouflage of foxholes. In this group, dermatitis varied in severity from erythema with mild swelling to large vesicles and more widespread redness. One man had camouflaged his foxhole and had

1. Allen, P. H.: Poisonous and Injurious Plants of Panama, Am. J. Trop. Med. (supp.) **23**:3-76 (Jan.) 1943.

then proceeded to remove ticks from his genitals. The result was a marked swelling of the glans and the shaft of the penis.

The history and clinical appearance indicated a contact reaction of the eyes and skin to some noxious agent in the plants. Spread from one part of the body to another was thought to be caused by contaminated hands.

Since ocular pain was the most distressing symptom, treatment had to be directed toward its relief. Despite administration of 1 grain (13 mg.) morphine sulfate to each patient prior to arrival at the clearing station, no substantial analgesic effect was obtained. It was then reasoned that local dilution of the toxic substance was necessary. A lukewarm dilute solution of boric acid was used as an eyewash. Its application was repeated many times. Care was taken to catch the fluid escaping from the conjunctival sac. A piece of cotton pressed against the cheek was used for this purpose. Then, with the eyes closed, the external surface of the lids was washed with the same solution. The skin involved elsewhere on the body was bathed with copious quantities of dilute solution of sodium bicarbonate. The effect of this simple treatment was dramatic. Relief of pain was immediate and complete.

No particular rationale is offered for the use of solution of sodium bicarbonate except for its cleansing action. Solution of boric acid was used, first, for its mechanical cleansing action; second, for its diluent effect on the toxic agent, and third, for its recognized soothing effect as a constituent of the usually prescribed eyewash.

All casualties were evacuated to a nearby station hospital. It was later learned that the average stay in the hospital was three days. Treatment used in the clearing station was recorded on the individual medical field tag and was continued in the hospital in similar fashion. No complications occurred. The objective signs disappeared almost entirely during the short period of hospitalization.

The importance of preventive treatment is indicated by the immobilization of 13 men from a single company of infantry in two hours. It is conceivable that a larger number of soldiers could be made noneffective, an eventuality which might result in failure to accomplish their mission. This danger can be averted by familiarization of all ranks with the consequence of contact with local flora, such as "beach apple."

SUMMARY

Thirteen cases of conjunctivitis and dermatitis caused by a toxic plant are reported.

Pain was the most prominent symptom, and treatment was directed toward its alleviation. The intensity of the reaction and the short interval of time required to produce it were worthy of note.

The use of dilute solution of boric acid for the eyes and dilute solution of sodium bicarbonate for the skin was found effective.

The average stay in the hospital was three days, and no complications occurred.

Preventive measures are stressed. Troops serving in areas infested with this plant should be warned of its harmful effects.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

ALKALI BURNS OF THE EYE

I. Review of the Literature and Summary of Present Knowledge

WILLIAM F. HUGHES Jr., M.D.
BALTIMORE

THE serious nature of alkali burns of the eye was first emphasized in 1813 by George Beer, who stated:

> . . . extensive and intensive chemical injuries of the eye are produced by slaked and unslaked lime . . . often acting so destructively that the entire cornea is disintegrated and suddenly changed into a greyish pulp which can be washed away from the iris below with a brush. . . . The effect of the mineral acids, if they are also as saturated, is rarely so destructive for the cornea as is unslaked lime.

Since then, these burns have been the subject of intensive study, and a number of papers have appeared on the pathologic and the chemical changes produced in the corneal stroma by alkalis. In regard to treatment there are two sharply conflicting schools of thought, one school advocating conservative treatment with irrigations, neutralizing agents, symptomatic therapy and, later, corrective surgical measures when indicated, while the second school urges the immediate removal of all necrotized conjunctiva and replacement with a mucous membrane graft.

The purpose of this review is to summarize the present state of knowledge on this subject and to attempt an evaluation of the various investigations and treatments thus far reported. This is preliminary to reports of additional studies pursued at the Wilmer Ophthalmological Institute. The subject will be discussed under the following headings:

1. *Clinical and pathologic course of alkali burns of the eye*
2. *Factors governing the severity of the lesion*
   - (*a*) Character of the cation
   - (*b*) Concentration of the alkali
   - (*c*) Duration of the exposure
   - (*d*) p_H of the solution
   - (*e*) Speed of penetration
3. *Mechanism of Action*
   - (*a*) Production of heat

The work described in this paper was done in part under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

(*b*) Withdrawal of water
(*c*) Effect on corneal constituents
Collagen
Mucoid
Albumin
Inorganic salts
Stroma cells
(*d*) Toxic hydrolysates
(*e*) Necrosis of limbal vessels

4. *Treatment*
(*a*) Emergency measures—experimental results
(*b*) Later treatment—general principles
(*c*) Comparison of clinical results: conservative treatment versus Denig graft

CLINICAL AND PATHOLOGIC COURSE OF ALKALI BURNS

The outstanding papers dealing with the clinical and pathologic course of alkali burns are those of de Gouvea (1869), Guillery (1906), Wagenmann (review in 1911), Siegrist (1920) and Yoshimoto (1928). All these authors have agreed that the ultimate prognosis cannot always be estimated at an early examination, since in many cases of apparently mild burns late infiltrations, necrosis or ulceration of the cornea develops. Some of the factors which govern the severity of the lesion are discussed later. From a review of the literature and from studies at the Wilmer Institute, which will be reported in detail later, the most prominent characteristics of a severe alkali burn can be summarized in chronologic order, as follows:

Time	Characteristics
1-10 min.	Rapid penetration of alkali through cornea into anterior chamber; diminished tactile sensitivity of cornea; disintegration and sloughing of conjunctival and corneal epithelium; opalescent opacification of cornea; washed-out appearance of substantia propria with beginning disintegration of stromal cells; fragmentation of corneal endothelium; hyperemia of iris
2 hr.	Edema and ischemia of conjunctiva and limbal (corneoscleral) region of the eyeball; infiltration of polymorphonuclear cells into conjunctiva, episcleral tissues and periphery of cornea; corneal edema, giving rise to opalescent haziness of cornea, with wrinkling of Descemet's membrane ("striate keratitis"); exudation of serum into anterior chamber; Greef blebs and edema of ciliary processes
18 hr.	Beginning regeneration of corneal epithelium; marked corneal edema, loss of metachromatic staining of corneal mucoid, disappearance of stromal cells; increase of purulent infiltration into conjunctiva, cornea and anterior chamber; opacity of anterior capsular and subcapsular region of lens

24-48 hr.	Moderate mucopurulent discharge in cul-de-sac; intensification of opacification, edema and purulent infiltration of cornea; appearance of spindle-shaped cells at periphery of lesion; regeneration of corneal endothelium
3-6 days	Petechial hemorrhages in ischemic areas of conjunctiva; varying amounts of superficial corneal ulceration, without apparent progression of corneal infiltration or opacification; persistence of iritis
7-13 days	Stage of gradual recovery or progression of corneal opacification and ulceration; varying amounts of mucopurulent discharge from eye; formation of adhesions between severely burned portions of bulbar and palpebral conjunctivas; localized corneal infiltrates of polymorphonuclear and mononuclear cells, with ulceration over such areas; beginning vascularization of cornea from limbal vessels, superficial loops from unthrombosed conjunctival vessels or brush-like projections from deep scleral plexus in ischemic regions; continued proliferation of spindle-shaped cells in cornea; subsidence of corneal edema; improvement of iritis
14 days and over	Abatement or progression of symptoms previously described; great resistance of Descemet's membrane to perforation; healing of corneal ulceration by proliferation of opaque fibrous tissue and blood vessels Complications of severe burns: Symblepharon with overgrowth of cornea by a vascularized membrane; persistent, progressive or recurrent corneal ulceration, occasionally leading to perforation; permanent corneal opacification; staphyloma of cornea; persistent or exudative iritis, at times ending in phthisis bulbi, secondary glaucoma or cataract

FACTORS GOVERNING SEVERITY OF LESION

The severity of alkali burns depends slightly on the character of the cation but more on the concentration of the alkali, the duration of exposure, the *p*H of the solution and its penetrability. These factors will now be discussed.

Character of the Cation.—The severity of the lesion in alkali burns is not greatly influenced by the type of cation. After exposure to ammonia the damaged cornea initially appears opalescent. In contrast, sodium hydroxide, potassium hydroxide and, especially, calcium hydroxide may produce a porcelain white opacification of the cornea immediately after exposure (Guillery, 1906). The ultimate prognosis for ammonia burns, however, is at least as poor as is that for lye and lime (calcium oxide) burns. Vinogorov and Kopit (1936) found that, although sodium hydroxide and potassium hydroxide produced similar lesions, the latter were somewhat more severe. A comparison of the ocular reactions to various alkaline calcium derivatives by Leonardi (1927) revealed differences in rapidity of development and in intensity but not in type. He produced a "scab-like" opacification of the cornea with the following substances in the

exposure time indicated: calcium oxide, two minutes; calcium oxide with dye and fish glue, ten minutes; calcium silicate and cement, twenty minutes; mortar and argillaceous limestone, one hour.

In view of the repeated attempts of various investigators and clinicians to extract calcium from lime-burned corneas with the use of ammonium salts, it is interesting to note that 0.1 cc. of a neutral and isotonic solution of calcium chloride (1.7 per cent) can be injected intracorneally without damage to the tissue. In his review, Cramer (1930) stated that a 30 to 50 per cent solution of calcium chloride can be safely instilled into the eye. Pichler (1924) reported a case in which solid particles of a calcium chloride powder (containing 90 per cent calcium chloride, 2 per cent potassium chloride, 3 per cent calcium oxide and 5 per cent unknown materials) were blown into the eyes of a man. The particles embedded in the cornea were rubbed off, and the cornea healed promptly. There is little direct evidence that combinations of calcium with organic material or inorganic salts in the cornea are the cause of the poor prognosis or the permanent corneal opacification following lime burns (see later sections). It is much more likely that the main destructive action of lime is caused by the alkalinity, or high p_H, of the calcium hydroxide solution. The relative unimportance of the cation in alkali burns is in sharp contrast to the importance of the anion in acid burns (Friedenwald, Hughes and Herrmann, 1944).

Concentration of the Alkali.—It is difficult to estimate by a study of case histories the minimal concentration of various alkalis which will produce damage to the human eye, because the exact concentrations are usually unknown, the concentrations of the solutions are ordinarily far above the minimal tolerance of the eye and the exact degree of contact with the eye cannot be ascertained. Guillery (1906) produced opacities of the rabbit cornea within a few minutes by brushing on 5 per cent sodium hydroxide, 10 per cent potassium hydroxide or 25 per cent calcium hydroxide. These solutions, as well as 10 per cent ammonia (ordinary household strength), have been used by many investigators to produce standard devastating lesions for treatment experiments. Yoshimoto (1928) found that a few drops of fifth-normal (0.8 per cent) sodium hydroxide produced a transient opacity for three days, whereas the instillation of half-normal (2.0 per cent) sodium hydroxide resulted in perforation of the cornea in seven days. For ammonium hydroxide, he found that a normal (3.5 per cent) solution produced a transient corneal opacity for three days; a twice normal (7 per cent) solution gave rise to an opacity lasting fourteen days, with only slight residual clouding, and a three times normal (10 per cent) solution produced a corneal ulcer with hypopyon which healed in eighteen days, leaving a dense corneal leukoma.

Duration of Exposure.—Much of the experimental work can be criticized from a quantitative standpoint, in that the instillation of only a few drops may be followed by reflex lacrimation, the tears diluting the alkali and washing it out of the eye. Clinically, the importance of the duration of exposure and the concentration of the alkali is emphasized by the ill effects which follow retention of solid particles of lye or lime hidden within the conjunctival folds of the eye. Unless such particles are completely removed the corneal opacification becomes progressively worse.

p_H of the Solution.—In experiments to determine the p_H tolerance of the cornea, Friedenwald, Hughes and Herrmann (1944) irrigated the eyes of rabbits for ten minutes and made intracorneal injections of a buffer solution of known and well established alkaline p_H. At higher p_H levels, dilutions of sodium hydroxide were used. These authors found that a p_H over 11.5, or 0.005 N (0.02 per cent) sodium hydroxide, would damage both the intact cornea and the corneal stroma.

Speed of Penetration.—Pichler (1910) instilled several drops of 10 per cent aqueous ammonia into the conjunctival sac of a rabbit. Ten minutes later the eye was enucleated and washed until no ammonia could be demonstrated in the wash water, and the aqueous withdrawn with a syringe was found to give a strong reaction for ammonia with Nessler's reagent. Ammonia could still be demonstrated in the aqueous after two hours but was absent at five hours. Siegrist (1920) obtained a doubtful positive reaction of the aqueous with Nessler's reagent five seconds after the instillation of strong solution of ammonia, a distinct positive reaction after fifteen seconds and a strong positive reaction after thirty seconds. Berezinskaja (1937) found that sodium hydroxide penetrated into the anterior chamber within five minutes after the instillation of a 5 per cent solution into the conjunctival sac of rabbits. De Gouvea (1869) demonstrated the presence of calcium chemically in the anterior chamber within twelve hours after exposure to lime.

MECHANISM OF ACTION OF ALKALI BURNS

Much speculation and experimental work have centered on a search for the causes of late infiltrations and ulceration of benign-looking alkali burns and the progressive nature of more severe burns.

Production of Heat.—The evolution of heat from dissolving calcium oxide or concentrated alkali solutions in water or tears has been considered a possible source of additional damage to the ocular tissue. Andreae (1899) found that it required ten to fifteen minutes before the slaking process of solid lime in the eye would produce a temperature over that of the blood. Lacrimation would tend to dilute the lime and lower the temperature. After the instillation of calcium oxide

into the conjunctival sacs of rabbits, measurement of the temperature by thermoelectric methods show no rise over 42 C. with the lids open or over 45 C. with the lids closed (Rosenthal, 1902). The temperature of the normal conjunctival sac of the rabbit has been reported by von Michel to be 32 C. Such a small increase in temperature could not damage the ocular tissues. Application of a thermophore at 45 C. is tolerated by the human cornea.

Withdrawal of Water.—Concentrated alkaline solutions, especially ammonia, have a strong affinity for water. It has been stated repeatedly in the literature that this property results in a withdrawal of essential water from the tissues. However, no experimental evidence can be found to support this hypothesis.

Effect of Alkali Burns on Chemical Constituents of the Cornea.—Alterations in the chemical constituents of the cornea following exposure to alkali have been investigated in some detail by Rosenthal (1902), Pagenstecher (1905), zur Nedden (1906), Guillery (1906), Haurowitz and Braun (1922) and Braun and Haurowitz (1923). Since the epithelium and endothelium make up only about one ninth of the weight of the cornea, the chemical analyses have largely represented changes in the corneal stroma. Krause (1934) tabulated the values for the chemical composition of the normal beef cornea, which may be summarized as follows:

Constituents of Beef Cornea	Percentage by Weight
Water	81.1
Inorganic matter (ash)	0.2
Organic matter	18.7
Water-insoluble proteins	18.4
Collagen	15.1
Mucoid	3.0
Elastin	Trace
Water-soluble proteins (albumin and globulin)	0.15
Extractives (water soluble; e. g., sugar)	0.13
Lipids (ether soluble)	0.04

Corneal Collagen: Since collagen comprises about 80 per cent of the organic material of the cornea, it has been hypothesized by Pagenstecher (1905) that the corneal opacity in cases of lime burns is due to a calcium-collagen combination.

Haurowitz and Braun (1922), following the technic of Mörner, extracted all the mucoid from beef corneas with tenth-normal ammonia. The resulting preparation consisted almost entirely of corneal collagen and was proved to be free of reducing sugars by testing with Fehling's solution after hydrolysis. Treatment of this preparation with lime resulted in some absorption of calcium, demonstrable chemically. These

corneas, devoid of mucoid but containing collagen, lost their swelling capacity after treatment with lime but did not show any reduction in translucency (the latter being also demonstrated by Mörner). Zur Nedden (1906) found that the addition of lime water to various commercial collagens produced no opacification. Haurowitz and Braun (1922) noted that alcohol-precipitated gelatin was dissolved by sodium hydroxide but not by ammonia or lime.

Corneal Mucoid: Mucoid (hyaluronosulfuric acid, or mucopolysaccharide) comprises about 20 per cent of the organic material of the corneal stroma. According to Levene (1925), Meyer and Chaffee (1940) and others, the composition of the complex polysaccharide associated with the protein probably contains a relative proportion of 1 molecule of acetylhexosaminesulfuric acid and 1 molecule of glycuronic acid. As previously noted, this corneal mucoid can be extracted completely with tenth-normal ammonia (Mörner) and other alkaline solutions. Guillery (1906) found that supersaturated solutions of calcium hydroxide and calcium chloride precipitated mucoid. Haurowitz and Braun (1922) also found that ammonia extracts of corneal mucoid became somewhat cloudy after the addition of either lime water or sodium chloride, being cleared subsequently by the addition of hydrochloric acid. Mucoid was also absorbed on the particles of a lime emulsion. They mentioned the fact that the behavior of proteins is dependent on many quantitative factors, e.g., concentration, temperature, salt content, p_H and other physical-chemical factors. Therefore, it would be unwise to suppose that these in vitro phenomena are directly applicable to the in vivo behavior of mucoproteins. These authors (1922 and 1923) also extracted mucoid from beef corneas with tenth-normal ammonia, the remaining material showing neither traces of reducing sugars nor metachromatic staining of mucoid with mucicarmine (Mayer's carmine—ammonium hydroxide stain) or thionin. However, in lime-burned corneas which were subsequently subjected to extraction with ammonia, the Fehling reaction for reducing sugars remained positive and the metachromatic staining was retained. With ordinary fixation in solution of formaldehyde U.S.P. or alcohol, metachromatic staining was lost in normal corneas but not in lime-burned corneas. The authors concluded that lime alters a portion of the corneal mucoid, making it no longer extractable with ammonia.

Recently, estimations of mucoid in rabbit corneas damaged by various chemical agents have been made by (1) metachromatic staining with toluidine blue and (2) microchemical determinations of hexosamine by Meyer and Chaffee [1] on similarly treated corneas.

1. A detailed report of these examinations will be published separately by Dr. Karl Meyer and Miss Eleanor Chaffee.[1]

In table 1 is shown a marked loss of hexosamine twenty-four hours after ten minutes' irrigation with twentieth-normal sodium hydroxide, whereas equally opaque corneas resulting from ten minutes' [2b] irrigation with half-normal hydrochloric acid showed no appreciable loss of hexosamine. There was also a distinctly greater loss of metachromatic staining of the mucoid in corneas burned with sodium hydroxide when examined at the end of twenty-four hours. In these studies, it was found that many other necrotizing substances produced some loss of corneal mucoid. Since the loss does not occur immediately,

TABLE 1.—*Effect on Corneal Mucoid of Various Chemical Agents* *

Substance	Time	Percentage of Opacity	Percentage of Hexosamine	Loss of Metachromatic Staining
Normal cornea	..	0	1.31 †	—
Sodium hydroxide (N/20)	0	81	1.27	±
	45 min.	88	0.79	1
	2 hr.	88	1.30	2
	4 hr.	88	0.96	1
	8 hr.	94	0.96	2
	24 hr.	88	0.48 ?	3
	2 days	81	0.37	..
(Specimen dried)	2 days	92	0.19	..
	4 days	88	0.34	..
	6 days	90	0.28	4
Hydrochloric acid (N/2)	1 hr.	66	1.23	0
	13-hr.	84	1.17	0
	24 hr.	92	1.29	0
(Dried)	24 hr.	84	1.03	..
	2 days	100	1.22	..
	4 days	88	1.21	..
	6 days	90	1.11	3
(Dried)	6 days	92	1.01	..
Toluidine blue (0.5%)	24 hr.	75	1.34	..
	6 days	81	1.07	(partial)1
Turpentine (nonspecific inflammation)	2 days	58	1.01	2
Mechanical edema (produced by damage to endothelium)	2 days	66	0.91	2 (?)

* The determinations of hexosamine were performed by Dr. Karl Meyer and Miss Eleanor Chaffee and will be reported on in detail by them elsewhere.

† Standard deviation = 0.15.

it may be related to secondary influences, e.g., corneal edema, damage to possible sources of hexosamine synthesis, inflammatory cells or proliferation of fibrous tissue.

In summary, there appears to be an early loss of corneal mucoid following sodium hydroxide and ammonia burns, contrasting sharply with the absence of an appreciable loss with acid burns. Haurowitz and Braun reported that exposure to lime results in an alteration of a portion of the corneal mucoid which prevents its extraction with ammonia and alcohol but does not interfere with its metachromatic staining with mucicarmine or thionin.

Albumin: Since there is only a trace of water-soluble proteins (albumin and globulin) in the cornea, it would be unlikely that an alteration in these constituents could account for much of the corneal lesion. Andreae (1899) obtained a precipitate on adding lime to hen egg albumin. However, zur Nedden (1906) and Guillery (1906) prepared a heavy suspension of albumin from egg and serum, taking precautions to exclude contamination with carbonate, and found that the addition of lime water or "lime brew" produced no cloudiness or precipitation.

Corneal Elastin: Krause (1934) found a small amount of elastin in beef cornea. With respect to a possible alteration in this component, Pagenstecher (1905) observed that the fibrillae of the cornea became straight after calcium burns (instead of being wavy), apparently having lost their ability to contract.

Lipids: The possibility that alkalis might saponify the trace of lipidal substances in the cornea was suggested by Leonardi (1927). There is apparently no experimental support of this hypothesis.

Formation of Insoluble Carbonates: The relatively dense corneal opacity following lime burns has been considered to be due, in part at least, to the deposition of calcium carbonate crystals. De Gouvea (1869) found that the addition of acid to lime-burned corneas gave an evolution of gas bubbles, presumably from the reaction of acid and calcium carbonate. Zur Nedden (1906) also obtained gas bubbles from the addition of hydrochloric acid to slices of fresh lime-burned corneas, and Guillery (1906) confirmed this, taking care to use carbonate-free lime in burning the corneas. Zur Nedden immersed beef corneas denuded of epithelium in distilled water for three days, after which they appeared opalescent and swollen but contained no dense opacity. Addition of lime water to these corneas did not produce any dense opacification, the soluble carbonates normally in the cornea apparently having diffused out. In corneas immersed in a 0.15 per cent solution of sodium bicarbonate for three days dense white opacification developed after treatment with lime water. Control corneas immersed in distilled water for three days and treated with heavy metals (lead, silver, copper, zinc or mercury) become opaque, the mechanism of opacification apparently being different from that with alkaline calcium solutions. The normal cornea contains only traces of inorganic salts: 0.2 per cent sodium carbonate, 0.8 per cent sodium chloride and 0.03 per cent phosphate and sulfate together. Because of these minute quantities, Pagenstecher (1905), zur Nedden (1906) and Guillery (1906) stated that calcium carbonate is probably deposited secondarily, the calcium being derived from calcium-protein combinations and the carbonate from the air and tissues. Wolff (1926) stated that he saw small white particles in the corneas of 2 patients with lime burns which

he considered to be deposits of calcium salts and which slowly disappeared within a few weeks.

Haurowitz and Braun (1922) found that with beef eyes denuded of epithelium an opacity was produced by the addition of alkaline solutions of calcium, barium and strontium salts but not of alkaline solutions of magnesium oxide and other alkalis or of neutral solutions of the alkaline earth salts. These investigators could demonstrate no gas bubbles on addition of hydrochloric acid to the burned corneas whether in fresh specimens, in corneas fixed with solution of formaldehyde U. S. P. or in corneas from which the mucoid had previously been extracted. However, lime-burned corneas fixed in alcohol gave a positive reaction to the bubble test with hydrochloric acid, indicating that the calcium carbonate was formed during the process of fixation in alcohol. They found that lime-burned rabbit corneas showed an immediate rise in calcium content to twice normal values but that the calcium disappeared from the burned corneas four weeks later, although the opacity remained. This was taken to indicate that the calcium ion was not directly responsible for the corneal opacification. This evidence does not rule out the possibility that the persistent corneal opacity might be due to fibrous tissue repair, even though the earlier opacity was related to the calcium ion. These authors could detect no precipitated phosphate after lime burns with use of the molybdenum reagent.

In conclusion, although it is possible that calcium ions in an alkaline medium might increase the early opacification of the cornea by precipitation with inorganic carbonates, it is unlikely that calcium ions per se accelerate the progress of the ocular lesion or contribute much to the intensity of the final corneal opacity.

Cellular Constituents: In addition to the changes in the extracellular collagenous material of the corneal stroma already outlined, consideration must also be given to the reaction of alkali with cellular constituents. One of the prominent features of alkali burns is the early disappearance of the stroma cells. What remains is completely devitalized tissue. It is possible, however, for new cells to grow into devitalized but otherwise uninjured corneal stroma. This may be seen in the reports of successful grafting of formaldehyde-fixed cornea. Burns with solid carbon dioxide result in temporary complete loss of all cellular structures in the affected area, with subsequent regrowth of new stroma cells and ultimate complete restitution of the normal histologic and clinical appearance of the cornea. It follows that the scarring, ulceration and other late changes which occur after alkali burns cannot be attributed solely to the initial destruction of cellular elements, but that some accompanying change in the collagenous or intercellular structure makes full recovery impossible.

Formation of Toxic Hydrolysates Following Alkali Burns.—Within a few hours after a severe alkali burn, polymorphonuclear cells appear within the conjunctival and episcleral tissues and rapidly penetrate into the substantia propria of the burned cornea. This inflammatory reaction is probably independent of secondary infection, because cultures and bacterial stains ordinarily reveal no pathogens during the first twenty-four hours following a chemical burn. The possibility that a toxic hydrolysate is produced by the action of alkali on the ocular tissues forms one basis for the emergency excision of necrotic conjunctiva and replacement with oral mucous membrane (Denig graft; see later section).

Necrosis of Limbal Vessels.—Alkali burns of sufficient intensity to render the limbal region ischemic are usually associated with grave corneal damage. Several clinical cases of chemical injury have been reported in which the initial changes apparently involved only the conjunctiva and sclera and infiltrations and ulceration developed later in the previously clear corneas (Denig, 1904; Thies, 1931, and Schmelzer, 1933). However, there is no experimental evidence that alkali burns involving the conjunctiva and sclera alone produce secondary corneal changes.

The epithelium and endothelium of the cornea are nourished by the bathing fluids with which they are in contact. It is not clear to what extent the viability of the corneal stroma is dependent on the limbal circulation and the diffusion of nutrient substances through the stroma. Mann and Pullinger (1942) reported that mustard gas (dichloroethyl sulfide) burns involving the limbus produce much greater damage to the cornea than burns caused by equal amounts placed on the center of the cornea or on the conjunctiva.

TREATMENT OF ALKALI BURNS OF THE EYE

Many problems arise in consideration of the proper treatment of alkali burns of the eye. Since alkalis penetrate into the anterior chamber within a minute or less after contact with the eye, surface decontamination by means of irrigations would have to be instituted immediately to prevent the development of any corneal lesion. After burns with solid lye or lime, repeated or later irrigations are of value in removing any residual particles of alkali which might be hidden within the conjunctival folds of the cul-de-sacs. The question arises whether first aid with weak acid or buffer solutions is superior to irrigations with water. For lime burns, solutions of various ammonium salts have been highly recommended to remove calcium from the burned cornea. However, it is doubtful whether such calcium deposits are harmful, or whether the ammonium salts effectively extract calcium from the cornea. The practicality of early paracentesis following

ammonia burns has not been properly evaluated. Many alkali burns respond favorably to conservative treatment, while others undergo progressive ulceration in spite of the emergency surgical removal of necrotic conjunctiva and replacement with oral mucous membrane (Denig graft). The experimental and clinical trials with the Denig graft have not been well controlled, and whether its reputed effectiveness is due to an enhancement of limbal circulation or to the removal of necrotized tissue is not clear.

The importance of secondary infection in alkali burns rests largely on the grounds that necrotic tissue furnishes a good bacterial medium and that positive cultures can be obtained from the conjunctival sacs. More recent methods of sterilizing the conjunctival sac have not been tried on eyes burned with alkali. The available experimental data on these questions will be discussed later, with a comparison of the results obtained clinically with conservative measures and with the Denig mucous membrane graft.

Experimental Results of Emergency Treatment.—1. Irrigations with Water or Neutralizing Solutions: In studies comparing the use of water and that of weak acid solutions (usually 1 or 2 per cent acetic acid) to remove or neutralize alkali which has not yet penetrated into the ocular tissues, most investigators have found that water is more effective (Andreae, 1898-1899; Rosenthal, 1902; Cosgrove and Hubbard, 1928; Leonardi, 1927; Brodskiy, 1938; Kaplan, 1939). Siegrist (1920) stressed the importance of immediate treatment after ammonia burns. He found that devastating lesions could be prevented by copious lavage with water only if performed within five seconds in young rabbits and within ten seconds in old rabbits after the instillation of 2 drops of strong solution of ammonia. Gurmann (1884, cited by Wagenmann, 1911) concluded from his experiments that carbon dioxide water was effective. Yoshimoto (1928) found that he could prevent perforating lesions and leukoma with the use of weak acid solutions or a 1 per cent solution of tannic acid within five minutes after exposure to alkali. In an unspecified number of rabbit eyes burned with 11 drops of 20 per cent sodium hydroxide instilled over a period of ten seconds, Hubbard (1937) found that "75 per cent of the alkali burns treated by irrigation with a weak acid were definitely better than the alkali burn of the opposite eye treated by irrigation with water alone."

In view of the fact that water is probably just as efficacious as weak neutralizing solutions and that speed in beginning treatment is of paramount importance, no time should be lost in an effort to obtain neutralizing antidotes instead of water. After burns with solid lye or lime, the use of weak acid solutions is of value in neutralizing small particles which escape removal by irrigation. For this purpose, the

following buffer solution is recommended because its stabilized p_H of 4.5 is well tolerated by the rabbit and the human eye:

Glacial acetic acid.....	2.9 cc. (0.05 molar)
Sodium acetate	6.8 Gm. (0.05 molar)
Distilled water, q. s.....	1,000 cc.

2. Solutions to Dissolve Calcium: Although it is doubtful that the serious prognosis or residual opacification of the cornea in cases of lime burns is due to the formation of insoluble calcium salts or calcium proteinates, several investigators, acting on the hypothesis that such deposits are formed, have utilized solutions of various ammonium salts in an effort to dissolve and extract such calcium precipitates. Guillery (1902) found that the amount of opacity in excised and in vivo corneas burned with lime was reduced by immersion in a solution containing 5 to 10 per cent ammonium chloride in 0.02 to 0.1 per cent tartaric acid. This solution dissolved mercuric albuminate and would, therefore, potentially dissolve any calcium proteinate. Applied as ocular baths of one-half to one hour's duration several times a day, this solution was found to be harmless for the normal human eye. Zur Nedden (1906) burned a portion of each of 16 pig corneas denuded of epithelium with lime and then soaked the specimens in 10 per cent solutions of 16 different salts chosen to dissolve any calcium precipitates. Corneas soaked in ammonium tartrate, ammonium chloride and ammonium chlorate became clearer after five minutes and entirely clear after three hours. Sodium or potassium tartrate did not completely clear the opacity after soaking for twenty-four hours. Ammonium tartrate also cleared corneal opacities due to lead, copper, zinc and aluminum. Early treatment of several lime-burned rabbit eyes with baths of 10 to 20 per cent ammonium tartrate or ammonium chloride twice daily resulted in clearing of the opacity in six to ten weeks. Old opacities covered by corneal epithelium cleared very little after such treatments. It should be remembered that opacification in rabbit corneas has a strong tendency to clear spontaneously, and zur Nedden did not report the severity of his control lesions nor the degree of spontaneous clearing. Gillessen (1926) found that the lime-burned eyes of 2 dogs treated with 10 per cent neutral ammonium tartrate showed better results than 1 control eye treated with a bland ointment. Alajmo (1929) reported that sodium citrate formed a more soluble and less dissociated calcium salt, and when used early in treatment experiments (rabbits), produced much better results than the tartrate. Antonibon (1931, cited by Pether) found that 8 per cent trisodium citrate was better than 10 per cent ammonium tartrate and that instillation had some beneficial effect even in old lesions. Pether (1939) compared the ability of various solutions to dissolve lime in vitro. He passed the various

solutions through 1 Gm. of calcium oxide at the rate of 182 cc. per minute and obtained the following results:

Substance	Molarity	Calcium Oxide Dissolved, Gm./Min.	Solution Value Relative to Water
Ammonium chloride	M	0.23	14.8
Ammonium tartrate	M/2	0.08	5.0
Ammonium acetate	M	0.07	5.0
Ammonium citrate	M/3	0.07	4.0
Sodium citrate	M/3	0.06	4.0
Boric acid	M/3	0.02	1.0
Sodium borate	M/6	0.01	1.0
Distilled water		0.01	1.0

A 1.2 per cent solution of ammonium chloride dissolved almost as much as a 9.2 per cent solution of ammonium tartrate; 0.026 Gm. of calcium carbonate dissolved in 100 cc. of the chloride solution after standing four hours, and 0.039 Gm. dissolved in the tartrate solution. However, he found that more lime dissolved in stronger concentrations of ammonium chloride and that a solution of 4 per cent could be used without irritation to the human eye. Braun and Haurowitz (1923) stated that calcium carbonate is 567 times as soluble in ammonium lactate as in ammonium tartrate and recommended iontophoresis with the lactate solution to facilitate pentration of the salt. Comparison of the results of iontophoresis of the two solutions using the eyes of 1 rabbit showed no difference in the eventual clearing of the lime opacity. In 2 rabbits with use of ammonium lactate iontophoresis, they found that the eye on which the positive pole was placed eventually became clearer than either the eye on which the negative electrode was placed or the control eye. This finding is somewhat inexplicable in that with the positive pole on the eye the ammonium ions would penetrate into the cornea.

3. Miscellaneous Emergency Measures: Schmidt-Rimpler (1900) recommended the instillation of oily drops to relieve the pain and cover the lime particles. Fortunati (1907, cited by Wagenmann, 1911) recommended the use of a 0.2 per cent trinitrophenol ointment. Sabata (1929) obtained unfavorable results in the treatment of lime-burned rabbit eyes using the following solutions: distilled water, 3 per cent boric acid, 10 per cent sugar solution, 1:4,000 solution of mercuric cyanate, isotonic solution of sodium chloride, 1:2,000 solution of tannic acid and 5 per cent sodium thiosulfate. Best (1930) obtained some favorable results with the use of glycerin and water (1:3) in the treatment of lime burns, the eyes first being cocainized. Utsumi and Endo (1937) reported 6 cases of severe burns with ammonia gas in which improvement followed treatment with a preparation containing a "detoxifying hormone of the liver," called Yakriton (Sankyo). In the abstract of this article no information is given of the method of preparing

Yakriton. Måhlén (1937) reported striking results in 13 patients treated with Pellidol (dimazon or diacetylaminoazotoluene salve). This substance is ordinarily used in 2 per cent concentration in a petrolatum base to stimulate the regeneration of epithelium in cases of chronic ulcers. Hubbard (1938) did not obtain any striking results in the treatment of sodium hydroxide burns of the rabbit eye with various solutions designed to provide a more leathery and drier surface and to prevent secondary infection: viz., 5 per cent tannic acid, 5 per cent tannic acid with 2 per cent silver nitrate, 1 per cent methylrosaniline chloride with 2 per cent silver nitrate and 1 per cent methylrosaniline chloride with 5 per cent tannic acid.

4. Paracentesis: When Pichler (1910) demonstrated ammonia in the anterior chamber within ten minutes after exposure, he suggested that an emergency paracentesis might, therefore, be of value therapeutically. Siegrist (1920) instilled 2 drops of strong solution of ammonia into both eyes of 3 rabbits and one-half to one minute later washed the eyes with a mildly acid solution. A paracentesis was then performed on one eye of each rabbit. Five days later, in the first rabbit the cornea of the eye operated on was entirely clear, whereas the control cornea was completely opaque; in the second rabbit there developed a diffuse, smokily opaque cornea with a small ulcer and hypopyon in the treated eye (no control eye); and the treated eye of the third rabbit showed a heavy opacity in the lower half of the cornea with only faint haziness of the upper half, as compared with the control eye in which there developed a deep yellowish white opacity of the entire cornea with perforation and prolapse of the iris. Since Pichler (1910) found that ammonia was still present in the anterior chamber two hours after the exposure but had disappeared in five hours, one would not expect a paracentesis to be effective after this interval.

Paracentesis has also been recommended by Middleton (1935) and Oaks (1945). The latter obtained pronounced clearing of initially opaque corneas in one eye burned with carbide (containing lime) and a second eye exposed to lye. The first aqueous obtained was opalescent, and paracenteses were repeated by depressing the corneal incision once or twice daily for about one week.

5. Denig Mucous Membrane Graft: This operation has been recommended for eyes in which the conjunctiva (especially near the limbus) is extremely necrotized and ischemic. Thies (1941) reserved its use for eyes with reduced sensitivity of the burned cornea. The technic of this operation has been given by Denig (1927), O'Connor (1933), Neuman (1935) and Thies (1938). First, the ischemic conjunctiva and episcleral tissue are completely removed along a 6 to 8 mm. strip adjacent to the limbus. Then, a strip of oral mucous

membrane is excised with scissors or the Graefe knife from the inside of the lower lip or cheek, a graft larger than the defect being obtained in order to allow for shrinkage. The epithelial side of the graft can be placed in contact with the gloved finger, and all excess submucous tissue should be trimmed off. The graft is then placed over the denuded sclera and sutured in place along the edges, with perhaps a stay suture through the superficial layers of the sclera and the central portion of the graft to hold it in close apposition with the sclera. A contact lens can be used for this purpose also. The eye is first dressed on the fourth or fifth day, at which time the superficial portions may appear necrotic and grayish white even though the graft is viable. Sutures are ordinarily removed about the twelfth or fourteenth day. Some of the complications which prevent a successful graft are (1) too deep and intensive necrosis of the sclera; (2) application of the graft too late after the injury, i. e., longer than six to eight hours; (3) bleeding under the graft; (4) secondary infection; (5) use of too small or too thick a graft, and (6) overriding of the burned cornea, resulting in adherence of the graft to the cornea.

Tissues other than oral mucous membrane have been used to replace necrotic conjunctiva or to correct symblepharon. Clay and Baird (1936) obtained good results with grafts from the prepuce and the labia minora respectively in 2 cases, but Siegel (1944) concluded from his experience with 3 grafts from the prepuce that they were "conspicuous, have a foul odor and desquamate." The latter author had excellent results in 5 out of 6 cases in which oral mucous membrane was used. De Rötth (1940) used fetal membranes obtained at cesarean section, placing the chorionic surface on the wound, with the amnion forming the free surface. These grafts in 8 cases showed a marked tendency to shrink, and the author reserved the use of this material only for cases in which oral mucous membrane was unobtainable. Brown (1941) inserted implants of rabbit peritoneum in order to prevent contact between burned palpebral conjunctiva and the cornea. These implants usually sloughed, and, in discussion of Brown's paper, Masters, Norris and Mann (1941) stated that the peritoneum itself could cause pressure necrosis of normal cornea. Wiener (1943) employed formaldehyde-fixed bovine conjunctiva to correct successfully a total symblepharon in 2 monkeys. From the cosmetic angle, conjunctiva is the most satisfactory tissue for grafting small defects, and this can be obtained from the upper cul-de-sac of the normal eye. Zenkina (1939) obtained conjunctiva from cadavers, not later than eighteen hours after death. The material was kept at a temperature of 2 to 4 C. in isotonic solution of three chlorides U. S. P. with 2 per cent dextrose for periods up to four days, and good results were obtained in 10 cases.

The Denig graft (using oral mucous membrane) has been used by its advocates in treating chemical burns of all degrees of severity. Many such burns would have responded equally well to conservative treatment (see compilation of statistics, p. 443). It has not yet been satisfactorily demonstrated that alkali burns strictly localized to the limbal conjunctiva and sclera will later involve the cornea, either because of necrosis of the limbal blood vessels or, possibly, because of a toxic hydrolytic product.

Later Treatment of Chemical Burns.—At present, the generally accepted later treatment for alkali burns of the eye may be summarized as follows:

1. Atropine: Iritis appears within twenty-four hours after any chemical burn which appreciably damages the cornea. The pupil should be dilated early by instilling a mydriatic, e. g., homatropine hydrobromide, 2 per cent, or atropine sulfate, 1 per cent. Although Palic (1928) found that in 26 out of 75 cases of alkali burns the intraocular tension increased, this should not contraindicate the judicious use of mydriatics to prevent posterior synechias.

2. Prevention of Secondary Infection: The importance of secondary infection in later ulceration of alkali-burned corneas has not been demonstrated. However, since pathogenic organisms are usually obtainable from culture soon after twenty-four hours have elapsed and necrotic tissue is considered to be a good medium for the growth of bacteria, the prophylactic use of chemotherapy would seem reasonable in all cases of corneal ulceration.

(*a*) Sulfonamide Ointments: Any of the sulfonamide compounds can be made into a satisfactory ophthalmic ointment by mixing finely ground powder into a bland base, such as petrolatum and hydrous wool fat. Sodium sulfadiazine and sodium sulfacetimide are preferable because of their effectiveness against common bacterial contaminants in the eye, their greater solubility in water, their higher penetrating power and the fewer local hypersensitivity reactions. Such an ointment, containing the drug in 5 or 10 per cent strength, should be instilled into the eye every three hours to maintain an adequate level of the sulfonamide compound in the ocular tissues. If the eye becomes irritated or if regeneration of the corneal epithelium appears retarded, the use of the ointment should be discontinued.

(*b*) Iontophoresis with Sodium Sulfadiazine or Sodium Sulfacetimide: Extremely high concentrations of sulfonamide compounds in the cornea and aqueous can be obtained with iontophoresis. Ordinarily, a 2.5 to 5 per cent solution of the sodium salt is placed within the glass iontophoresis container, which fits over the sclera like a contact lens. With the negative pole on the eye, a current of 2 milliamperes

from a 45 volt B dry cell battery is used for about three minutes. This may be repeated about every four hours when it is necessary to maintain a high level of the sulfonamide compound in the treatment of deep corneal ulcers or abscesses.

(*c*) Penicillin: The instillation of freshly prepared sodium or calcium penicillin (500 to 1,500 Oxford units per cubic centimeter in saline solution or per gram of petrolatum–wool fat ointment base) every few hours will sterilize the conjunctival sac of common ocular contaminants. Higher concentrations of sodium penicillin can be obtained in the cornea with the use of iontophoresis.

(*d*) Systemic Chemotherapy: For deep corneal ulceration and secondary endophthalmitis, the use of sulfadiazine or sulfamerazine orally or of sodium penicillin intramuscularly is recommended.

3. Prevention of Symblepharon: Severe alkali burns involving the conjunctiva in the cul-de-sacs frequently lead to permanent adhesions between the lids and the globe. Palic (1928) reported that in 31 of his 75 cases of alkali burns complete symblepharon developed. Measures which can be taken to combat this tendency include instillation of oily drops or ointment, frequent breaking of adhesions with a glass rod, insertion of a contact glass or use of a Denig mucous membrane graft. Unfortunately, if the burn has been sufficiently deep, the scarring will progressively obliterate the cul-de-sacs from below in spite of all prophylactic efforts. Permanent symblepharon can then be corrected by the resection of scar tissue and the use of oral mucous membrane or conjunctival grafts.

4. Improvement of Final Visual Acuity: The final reduction in vision is usually due to corneal opacification, irregular astigmatism and, at times, cataractous changes in the lens or secondary glaucoma. Often the irregular astigmatism can be corrected by the use of contact lenses. In suitable cases greatly impaired vision due to the corneal opacity can be improved with keratoplasty. The indications and technic for this procedure have been well outlined by Castroveijo (1941). In general, the reduction of visual acuity of both eyes should be below 20/200, the cornea should not be completely opaque, heavily vascularized or covered by symblepharon and there should be no anterior synechias or secondary glaucoma.

Clinical Results of Treatment of Alkali Burns.—Attempts to compare accurately the clinical results of different modes of treatment reported in the literature are difficult for the reasons that the exact degree of exposure to alkali cannot be determined and there are great variations in the time at which treatment was first instituted, in the technic of treatment and in the follow-up examinations of the patient. Essential data for the estimation of the initial severity of the burn are often

not given, and results are frequently classified as "good," "fair" or "poor." There is, also, an unfortunate lack of cases of bilateral ocular burns in which different methods of treatment have been employed on the two eyes. However, a clue to the relative merits of different technics migh be obtained by an examination of the reported cases. In addition, 34 cases of burns treated at the Wilmer Ophthalmological Institute are included.

The cases have been arbitrarily divided into three groups according to the initial severity of the burn. Cases of "mild burns include those in which the initial corrected vision was 0.5 or better or those in which the eye showed only an erosion of the corneal epithelium with faint haziness of the cornea and without any ischemic necrosis of the conjunctiva or sclera. Often it is impossible to obtain an accurate estimation of visual acuity on first examination, and so an estimation of the intensity of the corneal opacity gives a better index of the severity of

TABLE 2.—*Results of Treatment of Alkali Burns* *

No. of Cases	Severity of Burn	Treatment	Average Final Vision
23	Mild	Conservative	0.80
3		Denig graft	0.83
18	Moderately severe	Conservative	0.83 (S. D. = 0.22)†
9		Denig graft	0.33 (S. D. = 0.23)
10	Very severe	Conservative	0.13
13		Denig graft	0.30

* Summary of cases from the literature and unpublished cases from the Wilmer Ophthalmological Institute.
† S. D. indicates standard deviation.

the lesion. Cases of "moderately severe" burns include those in which the initial vision was 0.4 to 0.1, inclusive, or a corneal opacity was sufficiently dense to blur the details of the iris and fundus and minimal ischemic necrosis of the conjunctiva and sclera was present. In cases of burns classified as "very severe" the initial vision was less than 0.1, with blurring of the pupillary outline and blanching of the conjunctiva and sclera. In table 2 are included only those cases in which the burn was treated earlier than twenty-four hours after the injury, the majority of the burns having been treated by an ophthalmologist within a few hours after exposure. The greater number were due to lime, but a few lye and ammonia burns are included in each group. "Conservative treatment" includes all measures except the Denig graft, viz., irrigations; use of weak acid or buffer solutions, neutral ammonium tartrate or Pellidol; paracentesis, and abrasion of the cornea. In some cases the final vision was estimated from a description of the residual corneal opacity, according to the classification

of cases previously outlined. Follow-up periods varied from several weeks to several months, being essentially equal in the two groups.

The results in table 2 which includes cases from the literature and from Wilmer Institute, suggest that conservative measures may be more effective than the Denig graft for moderately severe alkali burns. The slight difference in favor of the Denig graft for very severe burns is not statistically significant.

Consideration of specific treatments for lime burns only is given in table 3. In the 11 cases of burns treated with "Pellidol salve" reported by Måhlén (1937) the corneas were described as initially more or less opaque, without any information as to how much the corneal opacity blurred the media or reduced the vision. Should these cases actually belong to group 3, or the group of "very severe" burns, the results of treatment would be even more striking. Ammonium tartrate appears to be as efficacious as the Denig graft in the treatment of very severe

TABLE 3.—*Treatment of Lime Burns* *

No. of Cases	Severity of Burn	Treatment	Average Final Vision
6	Mild	Irrigations, etc.	0.82
3		Ammonium tartrate	0.82
5		Pellidol	0.82
5	Moderately severe	Ammonium tartrate	0.68
6		Pellidol	0.80
2		Denig graft	0.20
3	Very severe	Irrigations	0.20
7		Ammonium tartrate	0.31
9		Denig graft	0.38

* Summary of cases from the literature and unpublished cases from the Wilmer Ophthalmological Institute.

lime burns, and several of the patients were not treated with tartrate until several days after the injury. Barkan and Barkan (1924) emphasized that the ammonium tartrate should be freshly prepared and neutralized. It is to be noted that their patients with severe lime burns treated with baths of this agent later required an "abrasion" of the cornea, an operation which the authors stated was made more successful by the previous treatment with ammonium tartrate. Most of their patients with very mild lime burns stated that the period of convalescence and the severity of symptoms were cut in half by the use of this solution. Wagenmann (1911) reported that in some of his patients the lime burns were made worse by treatment with ammonium tartrate and that there were no real beneficial results. De Rötth (1929) stated that 29 of his patients with alkali burns would have been considered by Denig and Thies as candidates for mucous membrane grafts but they recovered "good" vision on medical treatment alone. Seventeen patients with mild burns also recovered uneventfully, and 5 patients with very severe burns had final "poor" vision. Winkler (1939) treated 215 patients

with chemical burns (mostly lime burns) along conservative lines: irrigations of saline solution every hour for a while; a 2 per cent ethylmorphine hydrochloride salve; homatropine or scopolamine and hot compresses, with the eyes uncovered. Of these patients, 210 recovered, with completely usable vision, mostly 5/7 to 5/4 in each eye. One eye was lost as a result of extensive symblepharon, and 4 eyes with severe lime burns retained vision equivalent to ability to count fingers.

Neuman (1935) reported on a series of 50 cases of chemical burns treated by the Denig graft, the burn being considered "severe" in 30 cases and "very severe" in 20 cases and being caused by alkali in 27 cases (included in the previous tables). During this period, 79 mild burns did not receive a Denig graft. He compared the results in the 50 cases of severe burns with those in 105 cases in which the burns were treated conservatively prior to the time he began using mucous membrane grafts. His visual results were as follows:

No. of Cases	Treatment	No Light Perception	Visual Acuity				Symblepharon
			1/60	1/60-1/20	1/10-1/4	1/3-1	
50	Denig graft	18%	6%	10%	6%	60%	10%
105	Conservative	50%	8%	12%	7%	22%	52%

He stated that the best results with the Denig graft were obtained when the operation was performed within four hours after the injury. If it was done later than eight hours after injury, the final results were much worse. Among the 50 cases he reported 5 instances of "failure," evidently referring to the grafts which did not take. Berezinskaja (1940) used the Denig graft on 33 eyes, performing the operation one to twenty-two days after the burn. In 14 eyes the cornea cleared; in 3 eyes the cornea became transparent although the graft sloughed; in 4 eyes the cornea remained opaque, and 12 eyes became blind.

Zenkina (1939) obtained good visual results in 9 cases of alkali burns in which the oral mucous membrane used for transplantation was taken at autopsy fourteen to eighteen hours after death. The grafts were kept in Ringer solution with 0.2 per cent dextrose at 2 to 4 C. for twenty-four hours. All but 1 graft took well. Passow (1939) stated that he often dissected out the necrotic conjunctiva and closed the wound without using any graft. Klauber (1932) had 1 case of lime burn in which the corneal epithelium failed to regenerate until he transplanted a conjunctival graft from the opposite eye, four weeks after the injury.

SUMMARY AND CONCLUSIONS

The following summary and conclusions are derived from a review of the literature and from information obtained in studies pursued at the Wilmer Ophthalmological Institute.

Alkali burns are progressive in type, serious late complications frequently developing after little evidence of early involvement. The severity of the lesion is less dependent on the character of the cation than on the concentration of the alkali, the duration of the exposure and the p_H of the solution. The early dense white opacification in cases of lime burns may be due in part to the deposition of calcium carbonate, but it is doubtful whether the calcium ion per se affects the final prognosis. In contrast to acid burns, the mucoid content of the cornea decreases. After lime burns a part of the corneal mucoid is no longer extractable with ammonia.

Conservative treatment is effective for mild and moderately severe alkali burns. This consists of (1) immediate irrigation of the eye with copious amounts of water or any bland solution; (2) a thorough search and removal of any residual particles of alkali hidden within the conjunctival cul-de-sacs, followed by instillations of buffer solution (p_H 4.5); (3) instillation of mydriatics; (4) 10 per cent use of neutral ammonium tartrate (or lactate) as a corneal bath after lime burns (recommended in the literature); (5) instillations of sulfonamide or penicillin ointments to prevent secondary infection, and (6) prevention of symblepharon.

In a small number of reported cases in which early and repeated paracenteses were performed after chemical injury the ultimate clarity of the cornea was considered exceptionally good.

The early excision of necrotic conjunctival and episcleral tissue and its replacement with oral mucous membrane (Denig graft) or conjunctiva has been employed by many clinicians for the treatment of severe alkali burns. Analysis of these reported cases does not reveal any striking benefit attributable to such a procedure.

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Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Congenital Anomalies

THE CAUSE AND TREATMENT OF POOR VISION IN ANIRIDIA. L. G. ALGER, Am. J. Ophth. 28:730 (July) 1945.

Alger believes that the reduced vision associated with aniridia is due to aberration of light in the region of the equator of the lens. He discusses methods used to overcome this and reports a case in which he tattooed the cornea.

W. S. REESE.

MACULAR COLOBOMA WITH BILATERAL GROUPED PIGMENTATION OF THE RETINA. I. S. MCGREGOR, Brit. J. Ophth. **29:** 132 (March) 1945.

The anomalies indicated in the title of the article were present in the eyes of a fair-haired youth aged 19 years. In both eyes, all four quadrants of the fundus showed grouped pigmentation of the retina. The sectors or wedges of spots followed the main retinal vessels closely, and the shape of the spots varied from small black dots, near the disk, to larger and paler crescentic, round or polyhedral patches, which tended to fuse with one another nearer the periphery. The base of the wedge did not extend to the equator. In the right eye there was a roughly circular coloboma of the macula, much larger than the disk, with a nonpigmented base and a pigmented border. McGregor regards the condition in this case as a developmental, or inherent, fault, showing arrest and aberration, macular arrest and abnormal development of pigment as a somatic mutation.

W. ZENTMAYER.

Cornea and Sclera

ISOLATION AND IDENTIFICATION OF THE CAUSATIVE AGENT IN EPIDEMIC KERATOCONJUNCTIVITIS (SUPERFICIAL PUNCTATE KERATITIS) AND HERPETIC KERATOCONJUNCTIVITIS, A. E. MAUMENEE, G. S. HAYES and T. L. HARTMAN, Am. J. Ophth. **28:** 823 (Aug.) 1945.

The authors reach the following conclusions:

Herpes simplex virus can cause a keratoconjunctivitis which is clinically almost identical with that caused by the epidemic keratoconjunctivitis virus. In spite of the similarity in the clinical picture and the cross immunologic reactions of the two viruses, they are thought to be separate entities, but are probably of the same genus. Intranuclear inclusion bodies produced by the virus of epidemic keratoconjunctivitis have been demonstrated experimentally for the first time. Methylthionine chloride therapy for herpes and epidemic keratoconjunctivitis appears to be of some value in the early stages of these diseases.

W. S. REESE.

A Case of Interstitial Keratitis at an Early Age. P. J. Devlin, Brit. J. Ophth. **27:** 155 (March) 1945.

In a girl aged 15 months the eyes had become inflamed during the course of a heavy cold. The entire cornea of the right eye was opaque as a result of edematous and cellular infiltration, and a salmon-colored patch had developed. The condition of the left eye was similar; but the infiltration was less intense, and visible keratotic precipitates were present.

Results of the general physical examination were good except for "snuffles" and poor teeth. The mother's Wassermann reaction was positive.

W. Zentmayer.

The Use of Insulin in the Treatment of Corneal Ulcers. T. R. Aynsley, Brit. J. Ophth. **29:** 361 (July) 1945.

Aynsley reports 5 cases and refers to others of various types of ulceration of the cornea which responded favorably to the use of insulin, in 1 case when applied locally and in others when given by injection. The modus operandi of the insulin is suggested—the insulin improves the patient's nutrition; it removes some factor necessary for bacterial metabolism, or it increases the rate of epithelial proliferation.

W. Zentmayer.

Injuries

Clinical Signs and Therapy of Indirect Injuries of the Eye. Z. A. Kaminskaya, Vestnik Oftal. **22:** 7, 1943.

Indirect injuries of the eye were as frequent in the recent war as direct injuries. Kaminskaya analyzes cases of ocular injuries obtained chiefly as a result of trauma of the bones of the skull in the neighborhood of the eyeball. There are no external changes, but vision is frequently reduced to a greater degree than with penetrating wounds of the eye. Changes in the eye due to contusion arise most frequently from injuries of the lower lateral margin of the orbit.

The changes in the posterior segment of the eye follow the injury either immediately or later. Complete loss of vision is encountered in cases of large hemorrhages in the vitreous; the latter can occur either with perforation of the posterior limiting membrane or without. If the posterior membrane is not perforated, the vitreous is detached from the membrana limitans interna, and preretinal hemorrhages occur. There are also hemorrhages into the retina, near the optic disk or along the large blood vessels, as well as in the macular region. Edema of the macula occurs directly after trauma. The choroid is ruptured frequently with indirect trauma of the eye; the tear is irregular in shape, and a number of ruptures can be seen, indicating that the eye suffers a forceful injury. Injury to the retina is seen in the form of holes in the macula and detachment of the retina, though no detachment from the ora serrata has been observed.

The result of large hemorrhages in the vitreous is formation of bands of connective tissue and subsequent detachment of the retina, as well as synchysis scintillans. There were observed in the choroid

atrophic patches with pigment, the result of absorbed hemorrhages. Hypotonia of the eye is also one of the signs of the contusion syndrome.

The pathogenesis of contusion of the eyeball, according to Kaminskaya, lies in the spasm of the blood vessels (as is the case in the brain); in the later phase there is disturbance of permeability of the vessel wall with hemorrhages, followed by formation of connective tissue and secondary detachment of the retina.

The therapy of recent contusions of the eye consisted in the use of vasodilators. Later, since the vessel walls of the injured eye have a greater permeability than those of a normal eye, administration of calcium chloride was pushed in the form of intravenous and intramuscular injections and local ionization. Vitamin C had a beneficial effect. For the absorption of opacities in the vitreous, ionization with ethyl morphine hydrochloride, subconjunctival injections of the drug locally and blood transfusions were used, with favorable results.

O. SITCHEVSKA.

Neurology

ATROPHY OF OPTIC NERVE PRODUCED BY OPTICOCHIASMIC ARACHNOIDITIS. C. WESKAMP, An. argent. de oftal. **5:** 1 (Jan.-March) 1944.

Weskamp discusses fully the differential diagnosis of simple atrophy of the optic nerve and emphasizes that in those cases in which objective symptoms are absent and campimetric examination shows a central scotoma in addition to the characteristic peripheral contraction of the field the possibility of opticochiasmic arachnoiditis as the causative factor must be borne in mind. In such cases the ophthalmologist must be on guard and should call in consultation a neurosurgeon, as early operation is of the utmost importance.

Three cases are reported in which such a diagnosis was made through the teamwork of the ophthalmologist and the neurosurgeon. In 1 of the cases the condition was verified by operation.

H. F. CARRASQUILLO.

Orbit, Eyeball and Accessory Sinuses

THE OCULAR NEUROVEGETATIVE SYSTEM: NORMAL INTRAOCULAR TENSION. F. VIDAL and C. S. DAMEL, Arch. de oftal. de Buenos Aires **19:** 212 (April-May) 1944.

The authors examined 651 subjects with apparently normal eyes as to their intraocular tension. Tensions were taken but once, in the morning between 9 and 11. The Schiøtz and MacLean tonometers were used. According to their observations, physiologic tension ranges from 15 to 25 mm. (Schiøtz). The mean average physiologic tension is 19 mm. Lower tensions, down to 15 mm., belong to persons with physiologic ocular hypotension, and tensions higher, up to 25 mm., are classified as physiologic hypertension. There is a group of patients with unequal tension in the two eyes who deserve special study.

H. F. CARRASQUILLO.

Parasites

OCULAR SYNDROME IN ONCHOCERCIASIS. J. GRAHAM SCOTT, Brit. M. J. 1: 553 (April 22) 1944.

Onchocerca volvulus (the blinding filaria) is commonly found in certain parts of West Africa and America. It produces keratitis and iritis. Strong, Sanground, Bequaert and Ochoa (1934) found microfilarias in affected eyes. Hissette (1932, 1938) described chorioretinitis, retrobulbar neuritis and optic nerve atrophy in cases of onchocerciasis. Luna (1918, 1919) had previously described keratitis punctata onchocercosa due to filarial toxins.

Two cases of onchocerciasis are described in which (1) edema of the upper lid, (2) proptosis, (3) ciliary flush and (4) edema of the optic nerve occurred as unilateral phenomena. The cause is a lymphatic block due directly to microfilarias or indirectly to filarial toxins, as in Calabar swelling. One of these cases is believed to be the only instance of onchocerciasis reported in a Gambian, and the cause of the syndrome is an anaphylactic edema caused by O. volvulus. ARNOLD KNAPP.

Retina and Optic Nerve

THROMBOSIS OF THE RETINAL, CHOROIDAL, AND OPTIC-NERVE VESSELS. A. LOEWENSTEIN AND A. GARROW, Am. J. Ophth. 28: 840 (Aug.) 1945.

Eight cases form the basis of this paper, and the thrombotic changes were found in the vessels of the retina, of the optic nerve and of the choroid. Subendothelial fatty necrosis is frequent and may be found in the choroidal vessels as well. The veins and the arteries are usually involved in the changes.

A newly formed rete mirabile is stained sometimes with a dark blood stain. Chains of aneurysms may show fatty walls.

The central vessels in the optic nerve are often surrounded by a broad sheath of hyaline connective tissue with numerous elastic elements in it. A thrombus resembling a polypus was found in one artery, with lymphocytic infiltration of the wall of the nearby vein. In one artery a mass of exudate, which stained pink with eosin, was found external to a thickened internal elastic coat. The occurrence of a hemorrhage through a rupture in the wall of the vessel could be proved twice histologically. One organized venous thrombus showed endothelial giant cells.

Hemorrhage into the subdural and the subarachnoid spaces around the nerve is common. Some of the hemorrhagic areas are freely sprinkled with blood pigment.

Bruch's membrane may be damaged by a fatty infiltration, and in some places interrupted. Opposite one of these gaps there were damage of the external layers of the retina and a subretinal exudate. It is suggested that this is due to defective filtration through the damaged Bruch membrane.

In 3 of the cases spongy degeneration and cavitation of the optic nerve were found.

A sclerosed plaque was found in one optic nerve, with thrombosed small vessels near its margin, and the thrombosis of these small vessels

is probably the cause of the sclerosed plaque. The plaque may be similar to those found in disseminated sclerosis.

W. S. REESE.

News and Notes

GENERAL NEWS

Preceptorships.—With regard to the substitution of a preceptorship for a residency in an ophthalmic hospital, the American Board of Ophthalmology has always accepted such training in favorable cases. During the present overcrowding of facilities, the Board expects to take a liberal attitude regarding the requirements for training.

It should, however, be pointed out that neither a residency nor a preceptorship suffices in itself to meet the requirements of the Board. Each case will still be judged on its merits in determining fitness for examination.

In entering on a preceptorship, certain conditions should be kept in mind. First, the student will profit most after a sound course in the basic sciences of physiology of the eye and of vision, optics, pathology, bacteriology, chemistry, pharmacology, the relation of the eye to general disease, anatomy, embryology and neurology. This is essential for a residency, and more so for a preceptorship. While men have been accepted from preceptors not diplomates of the Board, it is obvious that the Board has more information about those teachers who have passed its examinations.

Any preceptor should understand that he is assuming responsibility in taking a student and is not merely obtaining help in the drudgery of his office. He should be willing to give time to clinical training and the use of apparatus, such as the slit lamp, ophthalmoscope and tonometer, and to direction of the student's surgical practice on animal eyes, assisting in operations and ultimately in the performance of them.

To cover the same amount of ground will take much longer in a preceptorship than in a residency, and students should accept opportunities to take hospital positions of all sorts as they become available.

Communications may be addressed to S. Judd Beach, M.D., secretary, Cape Cottage, Maine.

Gonin Medal Award.—The Gonin medal was presented on Nov. 3, 1945, to Dr. Paul Bailliart, of Paris, at the University of Lausanne in the presence of the family of Jules Gonin. There were also present Professors Amsler, Bückner, Goldmann, Franceschetti and Streiff; a large number of Swiss oculists, and, from foreign countries, Drs. Weve, Arruga, Faber and Mawas. Addresses were delivered by the rector of the University; by Professor Streiff, in the name of the Faculty of Medicine, and by the president of the Swiss Society of Ophthalmology.

This medal is bestowed every four years. It was given for the first time in 1941 to Professor Vogt.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.
Place: Habana, Cuba. Time: February 1948.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

FACULTY OF OPHTHALMOLOGISTS

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2, England.

GERMAN OPHTHALMOLOGICAL SOCIETY

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

MIDLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Mr. E. F. Wilson, 24 Upper Northgate St., Chester.
Secretary Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield 3.
Place: Manchester, Leeds, Newcastle-upon-Tyne, Liverpool, Sheffield and Bradford, in rotation. Time: October to May.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. J. Ringland Anderson, Astor House, 108 Collins St., Melbourne, Victoria.
Secretary: Dr. D. A. Williams, 27 Commonwealth St., Sydney.
Place: Melbourne. Time: Oct. 20-26, 1946.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF HOSPITAL DE NUESTRA SEÑORA DE LA LUZ

Chairman: Dr. Manuel J. Icaza y Dublán, México, D. F., Mexico.
Secretary: Dr. Jorge Meyrán, México, D. F., Mexico.

OPHTHALMOLOGICAL SOCIETY OF SOUTH AFRICA

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.
Place: London. Time: May 30-June 1-2, 1946.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1946.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Silvio de Almeida Toledo, Barão de Ilapetininga St., 88, 5° Andar, São Paulo, Brazil.
Secretary: Dr. Plinio de Toledo Piza, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmología del Norte

President: Dr. Alberto Cárdenas.
Secretary: Dr. Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4, III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: San Francisco. Time: July 1-5, 1946.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.
Place: Palmer House, Chicago. Time: Oct. 13-18, 1946.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.
Place: San Francisco. Time: June 26-28, 1946.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

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Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

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Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto 5.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Walter W. Wright, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. P. G. Spelbring, 131 S. Barstow St., Eau Claire.
Secretary: Dr. G. L. McCormick, 650 S. Central Ave., Marshfield.
Place: Gateway Hotel, Land O'Lakes. Time: May 18-19, 1946.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Theodore L. Terry, 140 Marlborough St., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston 16.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. James H. Mathews, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. A. R. McKinney, 330 S. Washington St., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnstown, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit National Bank Bldg., Dubois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month. October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON EYE, EAR, NOSE AND THROAT DISEASES

Chairman: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.
Secretary: Dr. Gabriel Tucker, 250 S. 18th St., Philadelphia 3.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Edmond L. Cooper, 1553 Woodward Ave., Detroit 26.
Secretary: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Karl C. Wold, 1051 Lowry Bldg., St. Paul 2.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul 2.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Harold M. U'Ren, 624 Medical Arts Bldg., Portland 5.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Secretary-Treasurer: Dr. Roderick Macdonald, 330 E. Main St., Rock Hill.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. E. B. Fairbanks, 315 Medical Arts Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Dean Spear, 516 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn 11.
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. William H. Howard, 389 Linwood Ave., Buffalo 9.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo 9.
Time: Second Thursday of each month from October to May.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Peter C. Kronfeld, 58 E. Washington St., Chicago 2.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.
Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.
Secretary: Dr. H. H. Wygand, Guardian Bldg., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.
Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.
Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Wesley G. Reid, 667 Fisher Bldg., Detroit 2.
Place: Club rooms of Wayne County Medical Society. Time: First Monday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Francis Carl Hertzog, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Robert G. Thornburgh, 117 E. 8th St., Long Beach, Calif.
Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.
Secretary-Treasurer: Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: James Robertson Hotel. Time: 6:30 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Rudolf Aebli, 30 E. 40th St., New York.
Secretary: Dr. Truman L. Boyes, 654 Madison Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Maurice L. Wieselthier, 1322 Union St., Brooklyn.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Secretary: Dr. S. R. Shaver, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. A. A. Steinberg, 1502 Farnam St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha 2.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Clarence F. Bernatz, Park Bldg., Pittsburgh.
Secretary: Dr. Robert J. Billings, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Isaac B. High, 326 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. Vincent Jones, 634 N. Grand Blvd., St. Louis.
Secretary: Dr. T. E. Sanders, 508 N. Grand Blvd., St. Louis 3.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey, 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secertary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. L. C. Ravin, 316 Michigan St., Toledo 2, Ohio.
Secretary: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.